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REVIEW PAPER

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Highlights of the 2019 Japanese Society of Hypertension Guidelines and perspectives on the management of Asian hypertensive patients

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Abstract

Unlike other international guidelines but in accord with the earlier Japanese Society of Hypertension (JSH) guidelines, the 2019 JSH guidelines ("JSH 2019") continue to emphasize the importance of out-of-office blood pressure (BP) measurements obtained with a home BP device. Another unique characteristic of JSH 2019 is that it sets clinical questions about the management of hypertension that are based on systematic reviews of updated evidence. JSH 2019 states that individuals with office BP < 140/90 mm Hg do not have normal BP. The final decisions regarding the diagnosis and treatment of hypertension should be performed based on out-of-office BP values together with office BP measurements. For hypertensive adults with comorbidities, the office BP goal is usually <130/80 mm Hg and the home BP goal is <125/75 mm Hg. Recommendations of JSH 2019 would be valuable for not only Japanese hypertensive patients but also Asian hypertensive patients, who share the same features including higher incidence of stroke compared with that of myocardial infarction and a steeper blood pressure-vascular event relationship.

1 | INTRODUCTION

Hypertension is one the most important risk factors for cardiovascular events worldwide. In Japan, cardiovascular events have had an impact on mortality that is similar to the impact of cancer. Adequate blood pressure (BP) control is thus critical for the prevention of cardiovascular events. The Japanese Society of Hypertension (JSH) first published its guidelines for the management of hypertension in 2000, and the guidelines were revised in 2004, 2009, 2014 (JSH 2014), and 2019 (JSH 2019).[1,2] As one of the unique characteristics is common to the previous JSH guidelines, the JSH 2019 guidelines continue to emphasize the importance of the use of out-of-office BP measurements obtained with a home BP device, unlike other international guidelines. Another unique characteristic of JSH 2019 is that it sets clinical questions regarding the management of hypertension, based on systematic reviews that clarified updated evidence. Several of those systematic reviews are described herein. JSH 2019 also refers to two major international guidelines, that is, the 2017 American College of Cardiology/American Heart Association guidelines (ACC/AHA) and the 2018 European Society of Cardiology/European Society of Hypertension (ESH/ESC) blood pressure guidelines, which were recently revised.[3,4] Here, we focus on the changes in JSH 2019 compared with JSH 2014 regarding the treatment of hypertension in clinical practice settings and offer perspectives on the management of Asian hypertensive patients.

2 | DEFINITION OF HYPERTENSION

In JSH 2014, individuals with office BP values <140/90 mm Hg were regarded as having normal-range BP. However, the term "normal-range" was removed in JSH 2019. In addition, the definitions of optimal BP (<120/80 mm Hg), normal BP (120-129/80-84 mm Hg), and high-normal BP (130-139/85-89 mm Hg) in JSH 2014 were replaced by normal BP, high-normal BP, and elevated BP, respectively, in JSH 2019 (Tables 1 and 2).

The authors of a Japanese cohort study reported that the lowest cardiovascular disease (CVD) incidence was in the population with office BP < 120/80 mm Hg, and the population with office systolic blood pressure (SBP) ≥ 140 mm Hg or office diastolic blood pressure (DBP) ≥ 90 mm Hg had a significantly greater risk of CVD compared with the population with office SBP < 120 mm Hg or office DBP < 80 mm Hg.[5,6] It was also reported that individuals with office BP 120-129/80-84 mm Hg and office BP 130-139/85-89 mm Hg had a significantly higher incidence of CVD compared with those with office BP < 120/80 mm Hg.[7] The use of the term "normal" in the JSH 2014 classification for office BP 120-139/80-89 mm Hg was thus suspected to result in a misunderstanding regarding the management of hypertension. Although the definition of hypertension does not change between JSH 2014 and JSH 2019, JSH 2019 emphasizes that both patients and physicians should be aware of the risk of hypertension at lower BP levels, and they should consider non-pharmacological therapy interventions including lifestyle modification. On the other hand, 2017 ACC/AHA guideline emphasize the diagnosis of hypertension as ≥130/80 mm Hg.[3] For not only Japanese population but also Asian population, earlier diagnosis of hypertension would be important, because stroke events are higher in Asian population than in Western population.[8] In addition, the contribution of increased BP for CVD events is also steeper in Asian population than in Western population.[9]

3 | OUT-OF-OFFICE BP MEASUREMENT

The JSH guidelines prior to 2019 emphasized the diagnosis and treatment of hypertension assessed by out-of-office BP measurement

TABLE 1 Classification of office blood pressure level in adults in JSH 2019

Classification	SBP		DBP
Normal BP	<120	and	<80
High-normal BP	120-129	and/or	80-84
Elevated BP	130-139	and/or	85-89
Grade I hypertension	140-159	and/or	90-99
Grade II hypertension	160-179	and/or	100-109
Grade III hypertension	≥180	and/or	≥110
ISH	≥140	and	<90

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; ISH, isolated systolic blood pressure; SBP, systolic blood pressure.

TABLE 2 Classification of office blood pressure level in adults in JSH 2014

Classification	SBP		DBP
Normal-range BP			
Optimal BP	<120	and	<80
Normal BP	120-129	and/or	80-84
High-normal BP	130-139	and/or	85-89
Hypertension			
Grade I hypertension	140-159	and/or	90-99
Grade II hypertension	160-179	and/or	100-109
Grade III hypertension	≥180	and/or	≥110
ISH	≥140	and	<90

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; ISH, isolated systolic blood pressure; SBP, systolic blood pressure.

(especially home BP measurement) as an adjunct to office BP (Figure 1). The recent US blood pressure guidelines also recommend this strategy for the management of hypertension. Several cohort studies revealed that compared with office BP, home BP was more strongly associated with the risk of CVD,[10-13] but the populations of most of the previous studies were limited to individuals in the general community.

Evidence obtained in studies of clinical populations concerning the association between home BP and CVD risk has emerged more recently. The Home blood pressure measurement with OImesartan Naïve patients to Establish Standard Target blood pressure (HONEST) study was a prospective observational study of 21 591 Japanese hypertensive patients who were followed for an average of 2.02 years.[14] The results of the HONEST study demonstrated that (a) home BP measurements taken in the morning were positively associated with CVD risk, and (b) the minimum-risk morning home BP level was 124 mm Hg as assessed by a spline regression analysis. In addition, the participants with morning home SBP ≥ 145 mm Hg and office SBP < 130 mm Hg were associated with CVD risk compared with the participants with morning home SBP < 125 mm Hg and office SBP < 130 mm Hg (hazard ratio [HR] 2.47, 95%CI: 1.20-5.08).

The Japan Morning Surge-Home Blood Pressure (J-HOP) study was a nationwide prospective observational study of 4310 Japanese with a history of or risk factors for CVD who were followed for 4 years.[15] The J-HOP results demonstrated that the morning home SBP values obtained during a 14-day period provided superior risk of incident stroke beyond the traditional risk factors (the C statistic value was increased from 0.756 to 0.802) in a model that included conventional CVD risk factors and office SBP. However, this improvement was significantly attenuated by the simultaneous assessment of morning and evening SBP (C statistic, 0.794). Thus, in Japanese hypertensive patients, home BP measurement—especially when performed in the morning—has been recommended for the management of hypertension.

Masked hypertension, which is elevated out-of-office BP despite normal office BP, is an important phenomenon with clinical significance. Since a number of studies have obtained evidence that home BP has stronger prognostic power than office BP, masked hypertension defined based on both home BP and office BP is naturally expected to present a risk of CVD. However, this evidence is not sufficient. In the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study, which was an observational analysis of 2051 residents of a town in Italy who were followed for 12.3 years, only two home BP measurements were performed at baseline.[16] The analysis (in an unadjusted model) revealed that compared with normotension (ie, home BP: <135 mm Hg SBP and <83 mm Hg DBP and office BP < 140/90 mm Hg), masked hypertension (ie, home BP: ≥135 mm Hg SBP or ≥83 mm Hg DBP, plus office BP < 140/90 mm Hg) was associated with a risk of CVD death. However, after adjustment for age and sex, this association disappeared.

The prognostic power of home BP measurement was also investigated in the Finn-Home study, a nationwide observational population study of 2046 participants in Finland.[17] The participants performed ≥14 home BP measurements and were followed for 7.5 years. For the study's definition of masked hypertension (9.2%), the current recommended cut-off BP levels of home BP (135/85 mm Hg) and office BP (140/90 mm Hg) were used. The unadjusted hazard ratio showed that masked hypertension was associated with a risk of cardiovascular events compared with normotension (HR 2.29, 95%CI: 1.42-3.68), but after adjustment for age and sex, this association disappeared (HR 1.39, 95%CI, 0.86-2.25).

In the J-HOP study,[18] we investigated whether masked hypertension defined based on home BP measurements presented a risk of stroke incidence in a Japanese clinical population. The results of our analyses revealed that masked hypertension posed a greater risk of stroke incidence compared with the controlled BP group after adjustment for traditional cardiovascular risk factors including office BP and cardiovascular end-organ damage (ie, urine

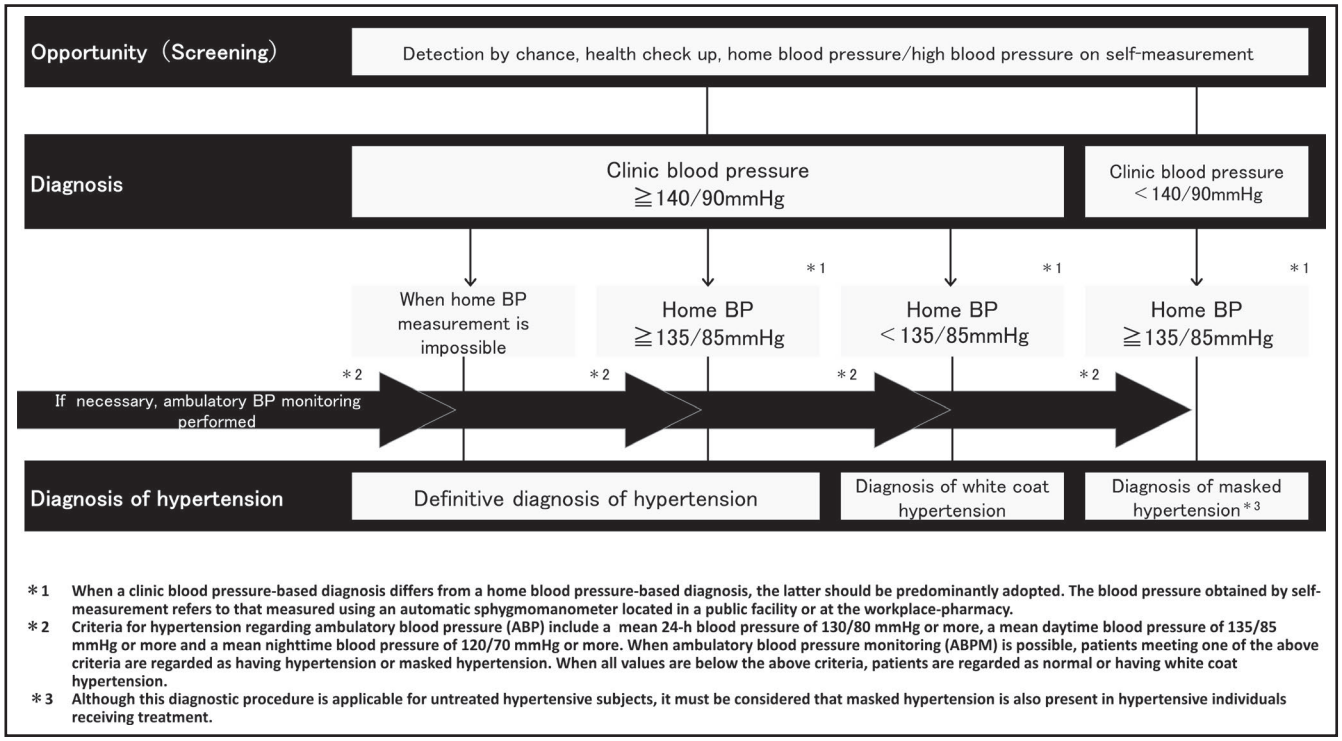

FIGURE 1 Blood pressure measurement and procedure for hypertension diagnosis. This figure is cited from JSH 2019 (*Hypertens Res*. 2019;42:1235-1481)

albumin-to-creatinine ratio [UACR] and circulating B-type natriuretic peptide) (HR 2.77, 95%CI: 1.20-6.37).[18]

In JSH 2019, the use of home BP measurement has focused on the diagnosis of masked hypertension as well as JSH 2014. One concern about the management of masked hypertension is that there has been no investigation of whether interventions for masked hypertension will help protect against target organ damage or reduce the risk of CVD. To address this concern, we recently performed a retrospective analysis using the combined data of two open-label multicenter randomized control studies: the Japan Morning Surge-1 (JMS-1) study[19] and the Japan Morning Surge-Target Organ Protection (J-TOP) study.[20] These two studies were designed to determine whether the participants could achieve <135 mm Hg home SBP, checked at 1-month intervals over a 6-month study period. Masked hypertension defined as ≥135/85 mm Hg morning home BP and <140/90 mm Hg office BP was observed in 133 patients, and sustained hypertension defined as both ≥135/85 mm Hg morning BP and ≥140/90 mm Hg office BP was observed in 570 patients. Both the office BP and the morning SBP of the patients with sustained hypertension fell significantly from baseline to the 6-month follow-up. In the patients with masked hypertension, the morning SBP had fallen significantly by the end of the follow-up period but the office SBP had not. In the patients with both masked and sustained hypertension, the degree of subclinical organ damage, the UACR, the brachial-ankle pulse wave velocity, and the left ventricular mass index were significantly reduced. In addition, there was no evidence of excessive office BP reduction in the patients with masked hypertension (Figure 2).[21]

Thus, although it is clear that out-of-office BP readings, especially home BP measurement, are definitely important for the management of hypertension in not only Asian population but also Western population. Although interventional prospective studies of masked hypertension are definitely needed, clinicians should be aware of the possibility of masked hypertension.

4 | BP CONTROL TARGET

Table 3 summarizes the results of the comparison of the BP control targets between JSH 2014 and JSH 2019. The target for BP control in a general population according to age in JSH 2019 is lower than that in JSH 2014 and was changed to <130/80 mm Hg for adults <75 years old and to <140/90 mm Hg for those ≥75 years old. The details of target BP control for adults ≥75 years old are provided below. Regarding individual <75 years old, the definition of hypertension is ≥140/90 mm Hg, and the BP control target for treatment is <130/80 mm Hg. This does not necessarily imply that individuals with 130-140/80-90 mm Hg should be treated with antihypertensive pharmacological therapy; if anything, JSH 2019 emphasizes that individuals with BP at 130-140/80-90 mm Hg and low risk should be treated with intensive non-pharmacological therapy. Pharmacological therapy should be considered for individuals with BP at 130-140/80-90 mm Hg with a high risk.

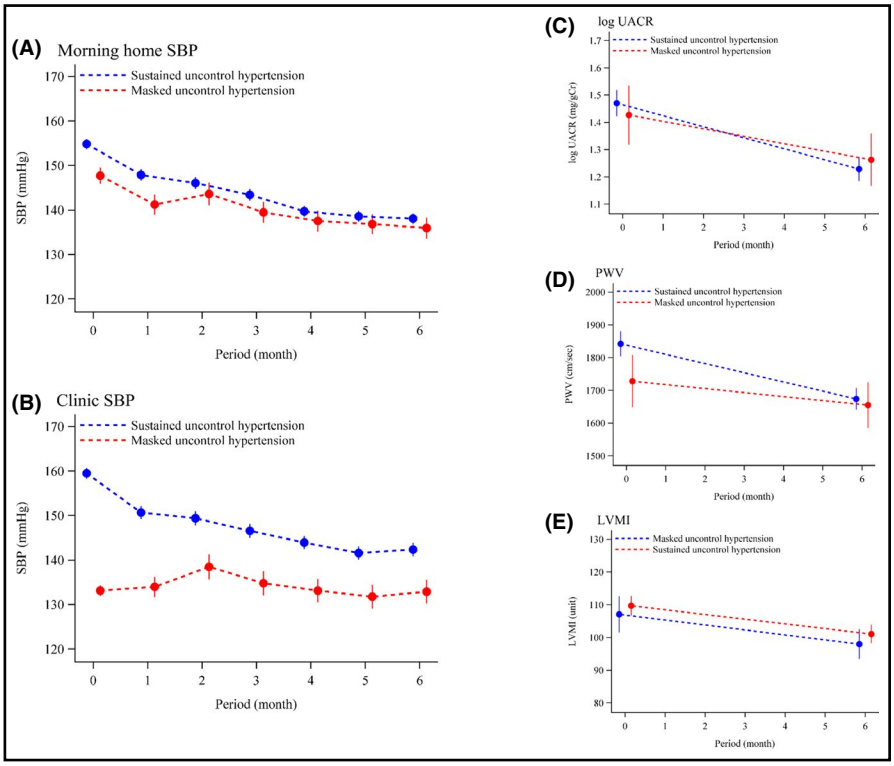

FIGURE 2 Changes in clinic SBP, home morning SBP, and the extent of subclinical CVD during the study period. This figure is original; the data are from *J Am Coll Cardiol*. 2018;71:2858-2859. The bars in panels (A, B) represent the adjusted means (SE) of clinic and home morning SBP at each month. The bars in panels (C-E) represent the adjusted means (SE) of log-transformed UACR, PWV, and LVMI, respectively, at baseline and 6 mo. The UACR levels were log-transformed because of their skewed distributions. PWV represents the average of the right and left baPWV. LVMI was calculated based on echocardiography following the ASE recommendations (*J Am Soc Echocardiogr.* 2015;28:1-39). LVMI, left ventricular mass index; PWV, pulse wave velocity; SBP, systolic blood pressure; UACR, urine albumin-to-creatinine ratio

The BP control targets for coronary artery and cerebrovascular disease in JSH 2019 are lower compared with those in JSH 2014. The lowered targets were influenced by the results of the Systolic Blood Pressure Intervention Trial (SPRINT)[22] and the Secondary Prevention of Small Subcortical Strokes (SPS3) study[23] as well as the 2017 ACC/AHA guidelines, which state that the BP goal for individuals with any comorbidities is <130/80 mm Hg. A major reason for the use of this value is provided by a systematic review included in JSH 2019 that analyzed six randomized control trials according to JSH 2014 and two other previous systematic reviews.[24,25] The findings demonstrated that the group of patients who achieved the BP control target (ie, 123-137 mm Hg) showed reduced all cause mortality (OR 0.73, 95%CI: 0.61-0.86) and reduced CVD mortality (OR 0.59, 95%CI: 0.45-0.76) compared with the patients who achieved higher target BP control at 135-149.7 mm Hg. However, the rates of composite CVD events and stroke incidence did not differ between these groups. There was also no significant between-group difference in the risk of adverse events (OR 1.02, 95%CI: 0.89-1.17).

The optimum home BP for a hypertensive individual has been defined as a value that is 5 mm Hg less than the office BP provided the office BP is already less than 140/90 mm Hg. Although there is insufficient evidence supporting this definition, the HONEST study showed that morning home BP at 124 mm Hg posed the minimum risk for CVD incidence. In addition, a sub-analysis of that study's population using home BP measurement showed that the CVD incidence was incrementally higher from the lowest risk in the group with <125 mm Hg morning home SBP to the groups with 125 to <135, 135 to <145, 145 to <155, and ≥155 mm Hg in the SPRINT high-risk population (ie, the patients with prevalent CVD, CKD, a Framingham CVD risk score ≥15%, or ≥75 years old) and in SPRINT-excluded high-risk population (patients with diabetes or prevalent stroke).[26] Therefore, 125/75 mm Hg as a target home BP value corresponding to 130/80 mm Hg as the target office BP value would be reasonable. Although the evidence for the benefit of strict BP control is not enough in Asian population, lower BP control would be important in not only Western population but also Asian population.

5 | BP TARGET FOR ELDERLY POPULATIONS

The aging of society is currently a global burden in Asian population and worldwide. The Japanese average life expectancy is the highest in the world (84.2 years old). In Japan, approx. 70% of the population with hypertension are elderly (≥75 years old). It is therefore important to design hypertension management for hypertensive elderly individuals, in Japan and elsewhere. In JSH 2014, the BP control target for treatment was 150/90 mm Hg in person aged >75 years, and if tolerated, the target BP goal was <140/90 mm Hg. JSH 2019 demonstrated that as a result of changing the 150/90 mm Hg target, BP control for the patients aged >75 years should be lowered to <140 mm Hg if tolerated.

The systematic review mentioned above included the SPRINT study, which largely contributed to the results of the systematic review.[27] In the SPRINT study, intensive BP control (<120 mm Hg SBP) significantly reduced the rate of CVD events compared with standard BP control (<140 mm Hg SBP). A similar result was observed regarding heart failure hospitalizations. In many countries, the incidence and prevalence of heart failure are increasing as a result of the

TABLE 3 Target levels of office and home blood pressure control in JSH 2019 and JSH 2014

	JSH 2019		JSH 2014	
	Office BP	Home BP	Office BP	Home BP
Adults with <75 y of age	<130/80 mm Hg	<125/75 mm Hg	<140/90 mm Hg	<135/85 mm Hg
Adults with ≥75 y of age	<140/90 mm Hg	<135/85 mm Hg	<150/90 mm Hg	<145/85 mm Hg
Comorbidities				
Diabetes mellitus	<130/80 mm Hg	<125/75 mm Hg	<130/80 mm Hg	<125/75 mm Hg
CKD without proteinuria	<140/90 mm Hg	<135/85 mm Hg	<140/90 mm Hg	<135/85 mm Hg
CKD with proteinuria	<130/80 mm Hg	<125/75 mm Hg	<130/80 mm Hg	<125/75 mm Hg
Coronary artery disease	<130/80 mm Hg	<125/75 mm Hg	<140/90 mm Hg	<135/85 mm Hg
Cerebrovascular disease	<130/80 mm Hg	<125/75 mm Hg	<140/90 mm Hg	<135/85 mm Hg
Using antithrombotic drugs	<130/80 mm Hg	<125/75 mm Hg	–	–

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

increasing elderly population. The majority of elderly heart failure patients have a preserved ejection fraction, and in contrast to heart failure with a reduced ejection fraction (HFrEF), there is no established treatment of the improvement of the prognosis of heart failure patients with a preserved ejection fraction (HFpEF). JSH 2014 mentions only that lower BP control is needed for the management of hypertension in patients with heart failure and a preserved ejection fraction.

In JSH 2019, a systematic review was performed to address whether a target SBP of <130 mm Hg should be recommended for patients with HFpEF.[28] The review of 11 randomized controlled trials revealed that the group with intensive treatment (reducing their SBP from 134.7 mm Hg to 130.2 mm Hg) had a significantly reduced rate of heart failure hospitalization compared to the group with standard treatment (SBP reduced from 134.4 mm Hg to 133.3 mm Hg; relative risk [RR], 0.89, 95%CI: 0.82-0.97). Based on those findings, JSH 2019 recommended that the SBP target for patients with HFpEF should be <130 mm Hg.

Blood pressure management using out-of-office BP may also be important for patients with HFpEF. We used ambulatory blood pressure monitoring (ABPM) for groups of patients with HFpEF (n = 232) and HFrEF (n = 276),[29] and the results showed that the riser BP pattern (ie, nighttime BP higher than daytime BP) was associated with the presence of HFpEF (OR 1.73, 95%CI: 1.02-2.91). Moreover, the ~21-month follow-up of the patients demonstrated that the riser BP pattern was associated with the risk of composite cardiovascular outcome (HR 3.01, 95%CI: 1.54-6.08) compared with the dipper BP pattern (nocturnal BP fall >10%). However, this association was not observed in the patients with HFrEF. The riser BP pattern and nighttime BP may be therapeutic targets for the reduction of CVD events among individuals with HFpEF.

Another concern in the management of hypertension in elderly populations is whether intensive treatment worsens cognitive function or dementia, because several papers implicated cerebral hypoperfusion in small vessel disease, which is a major risk factor for dementia.[30] In JSH 2019, a meta-analysis of 10 long-term prospective longitudinal observational studies reported that the risk of developing dementia was low in patients being treated with antihypertensive drugs (RR 0.86, 95%CI: 0.75-0.99). A sub-analysis of the SPRINT study patients showed that intensive treatment did not significantly reduce the risk of probable dementia compared with standard treatment, but it significantly reduced the risk of mild cognitive impairment (HR 0.81, 95%CI: 0.69-0.95).[31] We reported that the riser BP pattern was negatively associated with the brain matter volume assessed by brain magnetic resonance imaging (MRI), which itself was associated with cognitive function in 55 unmedicated elderly hypertensive patients (average age 72.7 years).[32] We also investigated the association between BP variability assessed by ABPM and cognitive function in 232 elderly patients (average age 77.7 years) with good BP control (24-hour BP, 118.7 ± 10.0/68.3 ± 6.4 mm Hg).[33] That study's results demonstrated that the top quartile of the weighted standard deviation (SD) of SBP as a measure of BP variability had a significantly lower total score on the Montreal Cognitive Assessment (MoCA) compared with the combined quartiles 1 through 3. Although the reason(s) for the association between BP variability and cognitive impairment are not yet known, exaggerated BP variability, that is, hemodynamic stress, may burden small cerebrovascular arteries and lead to artery damage and ischemia, which result in cognitive impairment.

However, more recently, a substudy of the SPRINT populations compared the changes in cerebral white matter lesions and brain volume assessed by brain MRI between an intensive-treatment group and a standard-treatment group.[34] In that study, 670 patients (mean age 67.3 years) underwent brain MRI at baseline and follow-up after a median period of 3.4 years. The results showed that the intensive-treatment group had a significantly smaller increase in cerebral white matter lesions and a greater decrease in total brain volumes compared with the standard-treatment group, although the differences in absolute values were slight. Thus, the association between intensive hypertension treatment and cognitive function/dementia remains a matter of debate. For Asian population faced to the aging of society, the recommendation of JSH 2019 for the treatment of hypertension on elderly patients would offer useful information.

6 | TREATMENT WITH ANTIHYPERTENSIVE DRUGS

JSH 2019 recommends that calcium (Ca) channel blockers (CCBs), angiotensin II receptor blockers (ARBs), angiotensin-converting enzyme (ACE) inhibitors, and diuretics should be selected as the first-line antihypertensive drugs. This recommendation is equivalent to those of JSH 2014. A study of an eastern Asian population reported that monotherapy with a CCB was more effective for BP reduction than other classes of antihypertensive drugs.[35] We surveyed health care practitioners and specialists in Asia and observed that 48% of them preferred a CCB as the best choice of antihypertensive drug for the first-line treatment of Asian hypertensive patients with no complications.[36] JSH 2019 recommends combination therapy with different classes of antihypertensive drugs to achieve the BP control target; for example, an ARB or ACE plus a CCB, or an ARB or ACE plus diuretics, or CCB plus diuretics.

Although it is not yet clear which combination is the best for hypertensive treatment, our previous findings may resolve this issue. The Japan-Combined Treatment With Olmesartan and a Calcium Channel Blocker Versus Olmesartan and Diuretics Randomized Efficacy (J-CORE) Study compared the effects of CCBs or diuretics used in combination with an ARB for the reduction of central SBP, and the results demonstrated that the combination of an ARB with a CCB significantly reduced central SBP compared with the combination of an ARB with diuretics, although there was no significant difference in peripheral SBP reduction assessed by ABPM between the two treatment groups.[37] Increased central SBP has been reported to pose a risk of cardiovascular events independent of peripheral SBP in Asian population.[38] Moreover, increased nighttime BP has prognostic power compared with daytime BP.[39,40] We compared the effects of the combination of an ARB plus a CCB and the combination of an ARB with diuretics on the reduction of nighttime BP assessed by a home BP device with ICT (information and communication technology) in Japanese hypertensive patients with nocturnal BP ≥ 120/70 mm Hg.[41] The results demonstrated that the combination of the ARB and CCB significantly reduced nocturnal BP compared with the combination of an ARB with diuretics. Thus, the combination of an ARB and a CCB may be preferable for treating Japanese hypertensives.

In JSH 2019, another notable issue regarding treatment with antihypertensive drugs concerns hypertensive patients with diabetes but not microalbuminuria or proteinuria. JSH 2019 recommends that CCBs, ARBs, an ACE inhibitor, or diuretics are the first-choice antihypertensive drugs; this recommendation differs from JSH 2014, in which only ARBs or ACE inhibitors recommended for this population. The JSH 2019 guidelines are based in part on the results revealed by a systematic review and meta-analysis of 16 studies that compared the cardiovascular outcomes afforded by renin-angiotensin system (RAS) inhibitors (ARBs or ACE inhibitors) with those provided by other antihypertensive drugs.[42] The RAS inhibitors tended to reduce the risk of cardiovascular outcomes compared with all of the other hypertensive drugs examined, but the difference was not significant (RR 0.93, 95%CI: 0.84-1.03 for CVD incidence; RR 0.84, 95%CI: 0.84-1.04 for cardiovascular mortality; RR 0.95, 95%CI: 0.85-1.05 for total mortality). In daily practice, combination therapy has been required in daily clinical practice.[43] Several evidence of combination therapy in Japanese hypertensive patients would be useful for other Asian population.

7 | CONCLUSIONS

JSH 2019 clearly states that individuals with office BP < 140/90 mm Hg do not have normal BP. The final decisions in the diagnosis and treatment of hypertension should be performed based on out-of-office BP measurements in conjunction with office BP measurements. For most hypertensive adults with comorbidities, the BP goals are office BP at <130/80 mm Hg and home BP < 125/75 mm Hg. Even in individuals over 75 years old, the optimal office BP target is <140/90 mm Hg, if tolerated. However, for elderly populations, tolerability is complicated, and physicians should therefore consider matters such as drug side effects, polypharmacy, organ damage, and quality of life when treating patients' blood pressure. Recommendation of JSH 2019 would be valuable for not only Japanese hypertensive patients but also Asian hypertensive patients, who share the same features including higher incidence of stroke compared with that of myocardial infarction and a steeper blood pressure-vascular event relationship.

CONFLICT OF INTEREST

K Kario received research grants from Omron Healthcare, A&D, and Fukuda Denshi Co. Ltd. S Park has received research grants and honoraria from Pfizer. T Kabutoya has received scholarship fund from Mitsubishi Tanabe Pharma Corporation. S Siddique has received honoraria from Bayer, Novartis, Pfizer, ICI, and Servier; and travel, accommodation and conference registration support from Atco Pharmaceutical, Highnoon Laboratories, Horizon Pharma, ICI, Pfizer, and CCL. YC Chia has received honoraria and sponsorship to attend conferences and CME seminars from Abbott, Bayer, Boehringer Ingelheim, GlaxoSmithKline, Menarini, Merck Sharp & Dohme, Novartis, Orient Europharma, Pfizer, and Sanofi; and a research grant from Pfizer. J Shin has received honoraria and sponsorship to attend seminars from Daiichi Sankyo, Takeda, Menarini, MSD, Bristol-Myers Squibb, and Sanofi. CH Chen has served as an advisor or consultant for Novartis Pharmaceuticals Corporation; has served as a speaker or a member of a speakers bureau for AstraZeneca; Pfizer Inc; Bayer AG; Bristol-Myers Squibb Company; Boehringer Ingelheim Pharmaceuticals, Inc; Daiichi Sankyo, Inc; Novartis Pharmaceuticals Corporation; SERVIER; Merck & Co., Inc; Sanofi; TAKEDA Pharmaceuticals International; and has received grants for clinical research from Microlife Co., Ltd. J Sison has received honoraria from Pfizer, AstraZeneca, Boehringer Ingelheim, and Novartis. GP Sogunuru has received a research grant related to hypertension monitoring and treatment from Pfizer. JC Tay has

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AUTHOR CONTRIBUTIONS

The contributions of the individual authors are summarized below. (1) Satoshi Hoshide MD PhD, Kazuomi Kario MD PhD, and Ji-Guang Wang MD PhD involved in conception. (2) Satoshi Hoshide MD PhD, Kazuomi Kario MD PhD, Naoko Tomitani BSc, Tomoyuki Kabutoya MD PhD, Yook-Chin Chia MBBS FRCP, Sungha Park MD PhD, Jinho Shin MD, Yuda Turana MD PhD, Jam Chin Tay MBBS FAMS, Peera Buranakitjaroen MD MSc DPhil, Chen-Huan Chen MD, Jennifer Nailes MD MSPH, Huynh Van Minh MD PhD, Saulat Siddique MBBS MRCP (UK) FRCP (Lon), Jorge Sison MD, Arieska Ann Soenarta MD, Guru Prasad Sogunuru MD DM, Apichard Sukonthasarn MD, Boon Wee Teo MB BCh, Narsingh Verma MD, Yuqing Zhang MD, Tzung-Dau Wang MD PhD, and Ji-Guang Wang MD PhD involved in drafting of the manuscript or critical revision for important intellectual content. (3) Satoshi Hoshide MD PhD, Kazuomi Kario MD PhD, Naoko Tomitani BSc, Tomoyuki Kabutoya MD PhD, Yook-Chin Chia MBBS FRCP, Sungha Park MD PhD, Jinho Shin MD, Yuda Turana MD PhD, Jam Chin Tay MBBS FAMS, Peera Buranakitjaroen MD MSc DPhil, Chen-Huan Chen MD, Jennifer Nailes MD MSPH, Huynh Van Minh MD PhD, Saulat Siddique MBBS MRCP (UK) FRCP (Lon), Jorge Sison MD, Arieska Ann Soenarta MD, Guru Prasad Sogunuru MD DM, Apichard Sukonthasarn MD, Boon Wee Teo MB BCh, Narsingh Verma MD, Yuqing Zhang MD, Tzung-Dau Wang MD PhD, and Ji-Guang Wang MD PhD involved in final approval of the submitted manuscript.

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REFERENCES

1. Shimamoto K, Ando K, Fujita T, et al. The Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2014). *Hypertens Res*. 2014;37:253-390.
2. Umemura S, Arima H, Arima S, et al. The Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2019). *Hypertens Res*. 2019;42:1235-1481.
3. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APHA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J Am Coll Cardiol*. 2018;71:2199-2269.
4. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens*. 2018;36:1953-2041.
5. Arima H, Tanizaki Y, Kiyohara Y, et al. Validity of the JNC VI recommendations for the management of hypertension in a general population of Japanese elderly: the Hisayama study. *Arch Intern Med*. 2003;163:361-366.
6. Ueda K, Omae T, Hasuo Y, et al. Prognosis and outcome of elderly hypertensives in a Japanese community: results from a long-term prospective study. *J Hypertens*. 1988;6:991-997.
7. Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: a cohort study. *Lancet*. 2001;358:1682-1686.
8. Ueshima H, Sekikawa A, Miura K, et al. Cardiovascular disease and risk factors in Asia: a selected review. *Circulation*. 2008;118:2702-2709.
9. Perkovic V, Huxley R, Wu Y, Prabhakaran D, MacMahon S. The burden of blood pressure-related disease: a neglected priority for global health. *Hypertension*. 2007;50:991-997.
10. Ohkubo T, Imai Y, Tsuji I, et al. Home blood pressure measurement has a stronger predictive power for mortality than does screening blood pressure measurement: a population-based observation in Ohasama, Japan. *J Hypertens*. 1998;16:971-975.
11. Niiranen TJ, Hanninen MR, Johansson J, Reunanen A, Jula AM. Home-measured blood pressure is a stronger predictor of cardiovascular risk than office blood pressure: the Finn-Home study. *Hypertension*. 2010;55:1346-1351.
12. Sega R, Facchetti R, Bombelli M, et al. Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the pressioni arteriose monitorate e loro associazioni (PAMALA) study. *Circulation*. 2005;111:1777-1783.
13. Asayama K, Thijs L, Brguljan-Hitij J, et al. Risk stratification by self-measured home blood pressure across categories of conventional blood pressure: a participant-level meta-analysis. *PLoS Medicine*. 2014;11:e1001591.
14. Kario K, Saito I, Kushiro T, et al. Home blood pressure and cardiovascular outcomes in patients during antihypertensive therapy: primary results of honest, a large-scale prospective, real-world observational study. *Hypertension*. 2014;64:989-996.
15. Hoshide S, Yano Y, Haimoto H, et al. Morning and evening home blood pressure and risks of incident stroke and coronary artery disease in the Japanese general practice population: the Japan Morning Surge-Home Blood Pressure study. *Hypertension*. 2016;68:54-61.
16. Mancia G, Facchetti R, Bombelli M, Grassi G, Sega R. Long-term risk of mortality associated with selective and combined elevation in office, home, and ambulatory blood pressure. *Hypertension*. 2006;47:846-853.

17. Hanninen MR, Niiranen TJ, Puukka PJ, Johansson J, Jula AM. Prognostic significance of masked and white-coat hypertension in the general population: the Finn-Home study. *J Hypertens*. 2012;30:705-712.
18. Fujiwara T, Yano Y, Hoshide S, Kanegae H, Kario K. Association of cardiovascular outcomes with masked hypertension defined by home blood pressure monitoring in a Japanese general practice population. *JAMA Cardiol*. 2018;3:583-590.
19. Kario K, Matsui Y, Shibasaki S, et al. An alpha-adrenergic blocker titrated by self-measured blood pressure recordings lowered blood pressure and microalbuminuria in patients with morning hypertension: the Japan Morning Surge-1 study. *J Hypertens*. 2008;26:1257-1265.
20. Kario K, Hoshide S, Shimizu M, et al. Effect of dosing time of angiotensin II receptor blockade titrated by self-measured blood pressure recordings on cardiorenal protection in hypertensives: the Japan Morning Surge-Target Organ Protection (J-TOP) study. *J Hypertens*. 2010;28:1574-1583.
21. Hoshide S, Yano Y, Kanegae H, Kario K. Effect of lowering home blood pressure on subclinical cardiovascular disease in masked uncontrolled hypertension. *J Am Coll Cardiol*. 2018;71:2858-2859.
22. Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103-2116.
23. Benavente OR, Coffey CS, Conwit R, et al. Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial. *Lancet*. 2013;382:507-515.
24. Weiss J, Freeman M, Low A, et al. Benefits and harms of intensive blood pressure treatment in adults aged 60 years or older: a systematic review and meta-analysis. *Ann Intern Med*. 2017;166:419-429.
25. Garrison SR, Kolber MR, Korownyk CS, McCracken RK, Heran BS, Allan GM. Blood pressure targets for hypertension in older adults. *Cochrane Database Syst Rev*. 2017;8:Cd011575.
26. Kario K, Saito I, Kushiro T, et al. Morning home blood pressure is a strong predictor of coronary artery disease: the HONEST study. *J Am Coll Cardiol*. 2016;67:1519-1527.
27. Takami Y, Yamamoto K, Arima H, Sakima A. Target blood pressure level for the treatment of elderly hypertensive patients: a systematic review and meta-analysis of randomized trials. *Hypertens Res*. 2019;42:660-668.
28. Kawano H, Fujiwara A, Kai H, et al. Effects of blood pressure lowering in patients with heart failure with preserved ejection fraction: a systematic review and meta-analysis. *Hypertens Res*. 2019;42:504-513.
29. Komori T, Eguchi K, Saito T, Hoshide S, Kario K. Riser pattern is a novel predictor of adverse events in heart failure patients with preserved ejection fraction. *Circ J*. 2017;81:220-226.
30. Wolters FJ, Zonneveld HI, Hofman A, et al. Cerebral perfusion and the risk of dementia: a population-based study. *Circulation*. 2017;136:719-728.
31. Williamson JD, Pajewski NM, Auchus AP, et al. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. *JAMA*. 2019;321:553-561.
32. Nagai M, Hoshide S, Ishikawa J, Shimada K, Kario K. Ambulatory blood pressure as an independent determinant of brain atrophy and cognitive function in elderly hypertension. *J Hypertens*. 2008;26:1636-1641.
33. Cho N, Hoshide S, Nishizawa M, Fujiwara T, Kario K. Relationship between blood pressure variability and cognitive function in elderly patients with good blood pressure control. *Am J Hypertens*. 2018;31:293-298.
34. Nasrallah IM, Pajewski NM, Auchus AP, et al. Association of intensive vs standard blood pressure control with cerebral white matter lesions. *JAMA*. 2019;322:524-534.
35. Wang JG, Kario K, Lau T, et al. Use of dihydropyridine calcium channel blockers in the management of hypertension in eastern Asians: a scientific statement from the Asian Pacific Heart Association. *Hypertens Res*. 2011;34:423-430.
36. Hoshide S, Wang JG, Park S, et al. Treatment considerations of clinical physician on hypertension management in Asia. *Curr Hypertens Rev*. 2016;12:164-168.
37. Matsui Y, Eguchi K, O'Rourke MF, et al. Differential effects between a calcium channel blocker and a diuretic when used in combination with angiotensin II receptor blocker on central aortic pressure in hypertensive patients. *Hypertension*. 2009;54:716-723.
38. Wang KL, Cheng HM, Chuang SY, et al. Central or peripheral systolic or pulse pressure: which best relates to target organs and future mortality? *J Hypertens*. 2009;27:461-467.
39. Kario K, Kanegae H, Tomitani N, et al. Nighttime blood pressure measured by home blood pressure monitoring as an independent predictor of cardiovascular events in general practice. *Hypertension*. 2019;73:1240-1248.
40. Boggia J, Li Y, Thijs L, et al. Prognostic accuracy of day versus night ambulatory blood pressure: a cohort study. *Lancet*. 2007;370:1219-1229.
41. Kario K, Tomitani N, Kanegae H, et al. Comparative effects of an angiotensin II receptor blocker (ARB)/diuretic vs. ARB/calcium-channel blocker combination on uncontrolled nocturnal hypertension evaluated by information and communication technology-based nocturnal home blood pressure monitoring- the nocturne study. *Circ J*. 2017;81:948-957.
42. Kunimura A, Himuro N, Fujiyoshi A, Segawa H, Ohnishi H, Saitoh S. The effects of renin-angiotensin system inhibitors on mortality, cardiovascular events, and renal events in hypertensive patients with diabetes: a systematic review and meta-analysis of randomized controlled trials. *Hypertens Res*. 2019;42:669-680.
43. Mori H, Ukai H, Yamamoto H, et al. Current status of antihypertensive prescription and associated blood pressure control in Japan. *Hypertens Res*. 2006;29:143-151.

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