Review

Key Points of the Japanese Society of Hypertension Guidelines for the Management of Hypertension in 2014

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Key Words

Japanese · Hypertension · Guideline

Abstract

The Japanese Society of Hypertension (JSH) published the new JSH guidelines for the management of hypertension in 2014, which is the revision of the JSH guidelines of 2009. The primary objective of the guideline is to provide physicians the standard treatment strategy of hypertension to prevent the hypertension-related target organ damage and cardiovascular events. The management of hypertension should be performed in hypertensive patients with a blood pressure of $\geq 140/90$ mm Hg. As Asians have a higher prevalence of stroke than of coronary artery disease and stroke is more steeply associated with the level of blood pressure, the target blood pressure should be lower than 130/80 mm Hg for high-risk patients such as those with diabetes or chronic kidney disease. Because of the increasing prevalence of obesity and the related metabolic syndrome, more salt intake and higher salt sensitivity in the population, lifestyle modifications are necessary in hypertensive patients and subjects with high normal blood pressure. This guideline provides evidence-based recommendations for the management of patients with hypertension with the characteristics of our society.

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Introduction

The Japanese Society of Hypertension published the new guidelines ‘The Japanese Society of Hypertension (JSH) Guidelines for the Management of Hypertension in 2014’ (JSH2014GL), aiming at a more effective prevention of hypertension-related organ damage and cardiovascular events in consideration of Asian characteristics (fig. 1) [1–4], which are different from

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Fig. 1. Characteristics of hypertension in Asia [4].

- 1. Stroke - more common than coronary artery disease**
- 2. Steeper association between BP and stroke**
- 3. High salt intake with high salt sensitivity**
- 4. Epidemic obesity and metabolic syndrome**
- 5. 24-hr BP control - more important**

Western characteristics, i.e., stroke occurs more often than coronary artery disease, the slope of the association between blood pressure (BP) and stroke is steeper, salt intake and salt sensitivity are higher, the prevalence of obesity and the related metabolic syndrome is increasing, the prevalence of non-dippers is high and 24-hour BP control is more important.

Making Process

The JSH2014GL chose 40 writing members and 79 document reviewers who were officials of the JSH and specialists in stroke, pregnancy-induced hypertension, endocrinology, dementia, dialysis, and medical economics. In addition, 15 liaison members were consigned based on recommendations from 14 affiliated societies, and evaluation was performed according to AGREE II (Appraisal of Guidelines for Research and Evaluation II) [5]. Eight advisors were consigned.

A systematic review was conducted. The post-JSH2009GL literature from January 2009 until June 2013 was investigated in PubMed using the key words ‘disease’, ‘target of blood pressure control’, and ‘selection of antihypertensive drugs’, and this was adopted as the basis of the systematic review. The results of the reassessment of the JSH2009 and ESH/ESC 2009, as well as references from the NICE/BHS guidelines in 2011 and ESH/ESC 2013, [6, 7] were presented to each member to reinforce literature investigation.

The evidence level and recommendation grade are shown in tables 1–3. With respect to the evidence level, epidemiological studies are high quality ones, but the evidence level is low (IVa) in the sense of intervention/treatment for hypertension. Therefore, for quotations that are not involved in the recommendation grade, E-Ia, Ib, II, and III were established, as presented in table 2. When guidelines prepared by other societies or positional statements were quoted, they were regarded as literature and expressed as (GL) without establishing the evidence level (tables 3, 4).

Measurement and Clinical Evaluation of BP

The importance of BP control throughout 24 h including sleep and morning periods was highly stressed in the JSH2014GL [1] as well as in recently published Western and international guidelines [6, 7], but not in two other guidelines [8, 9]. Both home BP monitoring and ambulatory BP (ABP) monitoring (ABPM) as well as office BP are recommended to use complementarily for the diagnosis of hypertension (fig. 2; table 5). Especially home BP monitoring is recommended to be used in clinical practice as the first step. In previous studies, home and ABPs are more closely associated with organ damage and cardiovascular prognosis than office BP in both hypertensive and community-dwelling Asian subjects [10–16].

Table 1. Classification of the evidence level regarding treatment/diagnosis

Evidence level	Classification
I	Systematic reviews, meta-analysis of randomized comparative studies
II	Randomized comparative studies
III	Non-randomized comparative studies, Subanalysis/retrospective analysis of randomized comparative studies
IVa	Epidemiological studies (cohort studies, meta-analysis of cohort studies)
IVb	Epidemiological studies (case-controlled studies, cross-sectional studies)
V	Descriptive studies (case reports, case series)
VI	Special committees' or specialists' opinions

Table 2. Classification of the evidence level of epidemiological studies regarding risk factors/prognosis

Evidence level	Classification
E-Ia	Meta-analysis of cohort studies
E-Ib	Cohort studies
E-II	Case-controlled studies, cross-sectional studies
E-III	Descriptive studies (case series)

Table 3. Recommendation grade described in POINT

Diagnosis/treatment items of POINT	
A	Strongly recommended based on strong scientific grounds
B	Recommended based on scientific grounds
C1	Recommended despite insufficient scientific grounds
C2	Not recommended despite insufficient scientific grounds
D	Not recommended based on scientific grounds
Important items were presented as POINT.	

Table 4. Rules for determining the recommendation grade

Diagnosis/treatment items of POINT	
A	There are ≥ 1 results at evidence level I (table 1)
B	There are ≥ 1 results at evidence level II (table 1)
C1/2	based on the results at evidence level III, IV, V, or VI (table 1)
D	There are ≥ 1 results at evidence level I or II (table 1)
Consensus-based recommendation grade is expressed as 'consensus'.

Fig. 2. BP measurement and procedure for hypertension diagnosis [1].

Table 5. Indications for ABPM

- 1 When a home BP fluctuates around 135/85 mm Hg or a clinic BP fluctuates around 140/90 mm Hg makes diagnosis of hypertension difficult.
- 2 When a high-normal value (125–134/80–84 mm Hg) is obtained on home BP measurement.
- 3 When there is marked variability in the home BP.
 - a. When a definitive diagnosis of white coat hypertension is not made based on the home BP level.
 - b. When a definitive diagnosis of masked hypertension is not made based on the home BP level.
 - c. When self-measurement of BP is impossible at the workplace and workplace hypertension is suspected.
 - d. When a definitive diagnosis of resistant hypertension is not made based on the home BP level.
 - e. When the nighttime BP is not measured on home BP and nocturnal hypertension (non-dipper, riser) is suspected.
- 4 When the information on short-term variability of BP is warranted.
 - a. When incidental, transient hypertension or hypotension is observed.
 - b. When the home and clinic BP levels markedly change.

When ABPM is possible in patients meeting one of the above indications, this should be performed if necessary.

Based on the discrepancy between the office and out-of office BPs, white coat hypertension and masked hypertension are diagnosed (fig. 3). Subtypes of masked hypertension are morning hypertension, nocturnal hypertension, and daytime hypertension (fig. 3). Morning hypertension and morning BP surge [17–24] as well as nocturnal hypertension and a riser pattern of nocturnal BP dipping [25–30] were demonstrated to be associated with cardiovascular risk in Asian studies.

Key Points

1. Clinic BP should be measured by maintaining the arm-cuff position at the heart level during rest in a seated position. The measurement must be performed two or more times

Fig. 3. Definition of white coat and masked hypertension.

at intervals of 1–2 min, and the mean value of two measurements that provide stable values (difference in the values: <5 mm Hg) should be used. Diagnosis of hypertension should be based on clinic BP measured on at least two different occasions. (Evidence level: VI.)

2. Clinic BP is measured by the auscultation method using a mercury sphygmomanometer, which is the standard procedure, but the use of an automatic sphygmomanometer is also permitted. (Evidence level: VI.)
3. Home BP measurement and 24-hour ABPM are useful for the diagnosis of hypertension, white coat hypertension, and masked hypertension, as well as for evaluating the drug effect and its duration. (Evidence level: IVa, III.)
4. Home BP should be measured with upper-arm devices. As a rule, it must be determined twice, and the mean value should be used as a BP value on the occasion. If the measurement is performed only once, the BP level should be used as a value on the occasion. (Evidence level: VI.)
5. Criteria for hypertension differ among clinic BP, 24-hour ABP, and home BP. A clinic BP of $>140/90$ mm Hg, a home BP of $>135/85$ mm Hg, and a mean 24-hour ABP of $>130/80$ mm Hg are regarded as indicators of hypertension. (Evidence level: E-Ia.)
6. When there is a discrepancy of diagnosis between clinic BP and home BP, a home BP-based diagnosis should have priority.
7. In treating hypertension, attention must also be given to the pattern of diurnal BP changes (non-dipper, riser, and dipper), nighttime BP, early-morning BP, and BP at the workplace. (Evidence level: E-Ib.)

White Coat Hypertension

1. Patients with a systolic clinic BP of >140 mm Hg and/or a diastolic BP of >90 mm Hg in whom systolic and diastolic home BPs are <135 and <85 mm Hg, respectively, or the

mean 24-hour systolic and diastolic BPs on ABPM are <130 and <80 mm Hg, respectively, are regarded as having white coat hypertension (fig. 3). (Evidence level: E-Ia.)

2. White coat hypertension is observed in 15–30% of hypertensive patients. In the elderly, the percentage increases. (Evidence level: E-II.)
3. White coat hypertension may deteriorate to hypertension and diabetes in the future. (Evidence level: E-Ib.)

Masked Hypertension

1. Patients with a mean systolic clinic BP of <140 mm Hg and a diastolic BP of <90 mm Hg who show a systolic home BP of >135 mmHg and/or a diastolic BP of >85 mm Hg, or a mean 24-hour systolic BP of >130 mm Hg and/or a diastolic BP of >80 mm Hg on ABPM are regarded as having masked hypertension (fig. 3). (Evidence level: E-Ia.)
2. Masked hypertension is classified into three types: early-morning hypertension (early-morning BP $\geq$ 135/85 mm Hg), nocturnal hypertension (nighttime BP $\geq$ 120/70 mm Hg), and daytime hypertension (daytime BP $\geq$ 135/85 mm Hg) (fig. 3). (Evidence level: E-Ia.)
3. Masked hypertension is observed in 10–15% of normotensive residents and in approximately 30% of hypertensive patients during antihypertensive therapy in whom systolic and diastolic BP levels are maintained at <140/90 mm Hg. (Evidence level: E-II.)
4. The risk of cardiovascular morbidity from untreated masked hypertension is similar to that from persistent hypertension. Masked hypertension should be regarded as a subtype of hypertension. (Evidence level: E-Ia.)

Principles of Treatment

The management of hypertension in accordance with the JSH2014GL should be performed in hypertensive patients with a BP of $\geq$ 140/90 mm Hg. In those with diabetes mellitus and chronic kidney disease (CKD) complicated by proteinuria, in which the risk of stroke, heart disease, and renal failure is high, hypertension treatment must be conducted if BP is $\geq$ 130/80 mm Hg. On the other hand, in hypertensive patients with metabolic syndrome, lifestyle modifications are necessary even in those with a high-normal BP (130–139/85–89 mm Hg). Even in normotensive patients, the prevention of hypertension through lifestyle modifications such as salt restriction, correction of obesity, and exercise is an important issue as a population strategy.

The most important difference between JSH2014GL and Western guidelines are the different target BP levels for high-risk patients with diabetes and/or CKD. Recently revised Western guidelines increased the target BP levels up to 140/90 mm Hg for these high-risk hypertensive patients [6–9]. As a characteristic of East Asian patients, the slope of the association between clinic BP level and stroke risk is steeper than that for Western patients [2–4]. In addition, as the phenotype of cardiovascular disease, stroke occurs more frequently than myocardial infarction [3, 4, 16]. Considering these Asian characteristics, in the JSH2014GL, the target BP levels remained at 130/80 mm Hg for high-risk hypertensive patients with diabetes and/or CKD with proteinuria (fig. 4). In addition, JSH2014GL recommended to achieve a home BP <125/75 mm Hg for hypertensive patients with diabetes (fig. 4) because two studies demonstrated the benefits of patients who could achieve this level [31, 32].

Key Points

1. Antihypertensive treatment should be performed to prevent the occurrence of cardiovascular disease due to sustained high BP, progression, recurrence-related mortality, and a reduction in the quality of life. (Recommendation grade: A; evidence level: I.)

	Clinic blood pressure	Home blood pressure
Young, middle-aged, and early-phase elderly patients	< 140/90mmHg	< 135/85mmHg
Late-phase elderly patients	< 150/90mmHg (<140/90mmHg if tolerated)	<145/85mmHg * (<135/85mmHg if tolerated)
Diabetic patients	< 130/80mmHg	< 125/75mmHg
Patients with CKD (with proteinuria)	< 130/80mmHg	< 125/75mmHg *
Patients with cerebrovascular diseases Patients with coronary artery disease	< 140/90mmHg	< 135/85mmHg *

Clinic BP should be < 130 mmHg in hypertensives with antiplatelet or anticoagulation therapy.

Fig. 4. Target levels of BP control (JSH 2014) [1].

- Antihypertensive treatment should be indicated for all hypertensive patients with a BP of >140/90 mm Hg. These patients are stratified into three groups: low-, moderate-, and high-risk based on the BP level, risk factors other than BP, and presence or absence of hypertensive organ damage.
- Antihypertensive treatment consists of lifestyle modifications (step 1) and antihypertensive drug therapy (step 2). The starting point of this therapy should be determined based on the risk level of the individual patients.
- The risk increases from the level of high-normal BP. Progression from high-normal BP to hypertension should be prevented by modifying the lifestyle. (Recommendation grade: B; evidence level: II.)
- The goal of antihypertensive treatment is to reduce the BP to <140/90 mm Hg. However, among diabetic and CKD patients with proteinuria, treatment should be performed in those with a BP of >130/80 mm Hg. The target BP is <130/80 mm Hg. In late-phase elderly hypertensive patients, the target BP is <150/90 mm Hg. If tolerance is present, a BP of <140/90 mm Hg should be targeted. (Recommendation grade: A; evidence level: I.)
- In principle, antihypertensive drug therapy should be started with a low dose of a long-acting drug once a day. If the dose must be increased, twice-daily administration may be considered. Appropriate combination therapy with antihypertensive drugs should be conducted to prevent adverse effects and enhance antihypertensive effects. Combination therapy should be considered from the outset for grade II or more severe hypertension. (Recommendation grade: B; consensus; evidence level: III.)
- Reducing the number of tablets and frequency of dosing is useful for improving adherence. (Recommendation grade: A; evidence level: I.)
- Home BP measurement is useful not only for the diagnosis of white coat hypertension and masked hypertension, but also for evaluating the antihypertensive effects or improving patients' adherence/concordance. (Recommendation grade: A; evidence level: I.)

9. Sufficient communication, information, and considerations for quality of life/adverse effects are useful for improving adherence, achieving better BP control, and preventing cardiovascular disease. (Recommendation grade: B; consensus; evidence level: IVa.)
10. For treatment, the attending physician must eventually determine a therapeutic strategy after establishing concordance involving the results of epidemiological and clinical studies, clinical background of the patient, pharmacological actions of antihypertensive drugs, health expenditure, and cost-effectiveness. (Recommendation grade: C1; evidence level: VI.)

Lifestyle Modifications

Asian subjects are likely to have a high salt intake with high salt sensitivity [4, 33]. Thus, salt restriction should be more effective in Asian patients than in Western patients.

Key Points

1. Lifestyle modifications are important for preventing hypertension as well as before and after the start of antihypertensive drug therapy. (Recommendation grade: A; consensus.)
2. Salt reduction: the target of salt reduction is <6 g/day. (Recommendation grade: A; evidence level: I.)
3. Dietary pattern: fruit/vegetable intake should be increased, and cholesterol/saturated fatty acid intake should be reduced. Fish (fish oil) intake should also be increased. (Recommendation grade: B; evidence level: II.)
4. Weight control: the target body mass index (BMI) is <25. Even when the target is not reached, a significant decrease in BP can be achieved by reducing body weight by approximately 4 kg. (Recommendation grade: A; evidence level: I.)
5. Exercise: primarily periodic (≥ 30 min daily if possible) and aerobic exercise should be practiced. (Recommendation grade: A; evidence level: I.)
6. Reduction of alcohol intake: alcohol intake should be restricted. (Recommendation grade: A; evidence level: I.)
7. Quitting smoking: smoking cessation should be promoted, and passive smoking must be avoided. (Recommendation grade: A; consensus; evidence level: IVa.)
8. Others: exposure to cold temperatures should be avoided. Emotional stress should be managed. (Recommendation grade: C1; evidence level: IVa.)
9. Comprehensive lifestyle modifications are more effective. (Recommendation grade: B; evidence level: II.)

Treatment with Antihypertensive Drugs

The JSH2014GL again stressed that BP lowering per se is more important than the different classes of antihypertensives. A recent meta-analysis of Asian clinical trials supported this statement [34]. The JSH2014GL separately used the words ‘major antihypertensive drugs’ and ‘first-line drugs’ and defined ‘first-line drugs’ as those that could be used in patients without any compelling indications. The major drugs included beta blockers; however, beta blockers are excluded from the first-line drugs.

Compelling indications are shown in figure 5. The RAS inhibitor is recommended to be used as the first-line drug for high-risk hypertensive patients with diabetes and/or CKD with albuminuria [35, 36]. The procedures of hypertension treatment in the absence of compelling indications are shown in figure 6. To achieve a target BP level, the combination of drugs are

	Ca antagonist	ARB/ACE inhibitor	diuretics	βblocker
LVH	●	●		
Heart failure		●	●	● *1
Tachycardia	● (nonDHP)			●
Angina pectoris	●			● *2
Old MI		●		●
CKD	Proteinuria–	●	●	
	Proteinuria+	●		
Chronic stroke	●	●	●	
Diabetes/MetS *3		●		
Osteoporosis			● (thiazide)	
Aspiration pneumonia		● (ACE –I)		

Fig. 5. Compelling indications [1].

Fig. 6. Procedures of hypertension treatment in the absence of compelling indications [1].

Fig. 7. Combination of two drugs [1].

recommended [37–39]; however, the combination of 2 RAS inhibitors [angiotensin-receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors] is not recommended (fig. 7).

Key Points

1. The preventive effects of antihypertensive drugs on cardiovascular disease are determined by the degree to which BP decreases rather than its class. (Recommendation grade: A; evidence level: I.)
2. Appropriate antihypertensive drugs should be selected considering compelling indications, contraindications, conditions that require the careful use of drugs and the presence or absence of complications. (Recommendation grade: B; evidence level: II.)
3. In hypertensive patients without compelling indications, the antihypertensive drug to be first administered should be selected from Ca channel blockers, ARBs, ACE inhibitors, and diuretics. (Recommendation grade: A; evidence level: I.)
4. Antihypertensive drugs are administered once a day, in principle, but as it is more important to control the BP over 24 h, splitting the dose into twice a day is desirable in some situations. (Recommendation grade: C1; evidence level: III.)
5. A gradual reduction in BP is desirable in hypertensive patients in general, but the target control level should be achieved within several weeks in high-risk patients, such as those with grade III hypertension and multiple risk factors. (Recommendation grade: C1; evidence level: III.)
6. The use of two or three drugs in combination is often necessary to achieve the target of BP control. (Recommendation grade: A; evidence level: I.)
7. Combination therapy with different classes of antihypertensive drug exhibits potent hypotensive effects and is useful for achieving the target of BP control. (Recommendation grade: A; evidence level: I.)

8. Among the combinations of two drugs, those of a renin-angiotensin (RA) system inhibitor (ACE inhibitor or ARB) + Ca channel blocker, RA system inhibitor + diuretic, and Ca channel blocker + diuretic are recommended. (Recommendation grade: B; evidence level: II.)
9. Simplification of the prescription using fixed-combination drugs is useful for improving adherence and controlling BP. (Recommendation grade: A; evidence level: I.)

Disclosure Statement

The author has no conflicts of interest to declare.

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