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2019 Chinese guideline for the management of hypertension in the elderly

Hypertension Branch of Chinese Geriatrics Society
National Clinical Research Center of the Geriatric Diseases-Chinese Alliance of Geriatric Cardiovascular Disease

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Abbreviations
AASI: ambulatory arterial stiffness index
ABPM: ambulatory blood pressure monitoring
ACEI: angiotensin converting enzyme inhibitor
AF: atrial fibrillation
AHI: apnea hypoventilation index
ANS: autonomic nervous system
ARB: angiotensin receptor blocker
BB: beta blocker
BMI: body mass index
BP: blood pressure
CCB: calcium channel blockers
CHD: coronary heart disease
CKD: chronic kidney disease
CPAP: continuous positive airway pressure
DBP: diastolic blood pressure
eGFR: estimated glomerular filtration rate
GFR: glomerular filtration rate
GRA: glucocorticoid-remediable aldosteronism
HBPM: home blood pressure monitoring
IHA: idiopathic hyperaldosteronism

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LVMI: left ventricular mass index
MI: myocardial infarction
NIPPV: non-invasive positive pressure ventilation
PA: primary aldosteronism
QoL: quality of life
RAS: renin-angiotensin system
RH: resistant hypertension
RVH: renovascular hypertension
SBP: systolic blood pressure
TOD: target organ damage

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Preamble

Population aging has been a great social challenge in China. By the end of 2017, there were 158.31 million people aged 65 years or over, accounting for 11.4% of all population in China. To meet this challenge and strive for the realization of "healthy aging", the Chinese government has translated its policy priority from "disease treatment" to "health promotion and disease prevention".

Hypertension is one of the most common chronic diseases in China. Over half of Chinese elderly people have hypertension, and for those aged 80 years or over, the prevalence reached 90%. Hypertension is the leading risk factor of stroke, myocardial infarction and cardiovascular mortality. During the past years, hypertension management in China has been improved significantly, with the control rate of hypertension in elderly patients increased from7.6% in the year of 2002 to 18.2% in 2015. However, this improvement is far from ideal, given the rapid economic and social progress in China and the great development in hypertension controlling worldwide. Most guidelines for the prevention and treatment of hypertension developed in various countries, including those developed in China, contains specific chapters for elderly patients, but the contents are usually limited. Management of hypertension in the elderly patients, a specific population, including prevention, diagnosis, evaluation and treatment strategy, however, is much different from those in younger patients. Thus, there is an urgent need to develop a clinic practice guideline focusing on the elderly people for further improving the quality of management of hypertension in Chinese elderly patients.

Supported by the Chronic Disease Control Department of the National Health Commission, the Hypertension Branch of Chinese Geriatrics Society, in conjunction with the National Clinical Research Center of the Geriatric Diseases-Chinese Alliance of Geriatric Cardiovascular Disease, organized a preparatory committee to develop this document in 2017. During the one and half years since this committee was organized, members of the committee had participated in literature reviewing, document planning, article writing, evaluation of evidence and recommendation classification, according to the international and national protocols of guideline development. Finally, the Guideline Writing and Review Committee organized several conferences to discuss and revise the contents relating to the measurement of blood pressure, the goals of blood pressure control in specific populations, blood pressure fluctuation, function preservation, multiple medications and other topics. In writing this guideline, the Committee has fully considered data from high quality clinical trials undertaken both in China and in other countries, but paying particular attentions to those in Chinese patients. "Chinese guideline for the management of hypertension in the elderly" is a guiding document with distinctive characteristics, closely related to clinic, combining practice and evidence, especially suitable for the management of elderly hypertensive people in China. We hope this guideline well be a help for the prevention and treatment practice of hypertension in elderly patients in China.

(Hua Qi, MD & Fan Li, MD)

1 Introduction

1.1 Class of recommendations and level of evidences

The class of recommendations and level of evidences are listed in the Tables 1 & 2.

1.2 Definition and categories of hypertension in the elderly

Hypertension in the elderly is defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg measured three times in different days among patients aged ≥ 65 years without any previous antihypertensive drugs treatment. If elderly patients have hypertension history, and they are now receiving antihyper-

Table 1. Class of recommendations.

Classes of recommendations	Definitions	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favor of usefulness/efficacy.	Should be considered.
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered.
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended.

Table 2. Levels of evidences.

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Table 3. Categories of BP and definitions of hypertension grade in the elderly.[1]

Categories	SBP, mmHg		DBP, mmHg
Optimal	< 120	and	< 80
High Normal	120–139	and (or)	80–89
Hypertension	≥ 140	and (or)	≥ 90
Grade 1 hypertension	140–159	and (or)	90–99
Grade 2 hypertension	160–179	and (or)	100–109
Grade 3 hypertension	≥ 180	and (or)	≥ 110
Isolated systolic hypertension	≥ 140	and	< 90

BP category is defined by the highest level of BP, whether systolic or diastolic. Isolated systolic hypertension is graded according to SBP values. BP: blood pressure; DBP: diastolic blood pressure; SBP: systolic blood pressure.

tensive drugs therapy, they should be diagnosed with hypertension in the elderly though the blood pressure (BP) < 140/90 mmHg. The categories of geriatric hypertension are the same with the categories of hypertension in adults (Table 3).

BP category is defined according to the seated office BP. In recent years, home BP monitoring (HBPM) and ambulatory BP monitoring (ABPM) have been widely used in China, which has become an important supplement for the BP measurement in the clinic office. However, the standardization and quality control of BP measurement equipment need to be further improved. At present, the results of BP measurement outside the office are not taken as an independent basis for the diagnosis of hypertension in the elderly.

1.3 Current status of epidemiology of hypertension in the elderly

The results of the national wide hypertension sampling survey in 1991 showed the prevalence of hypertension in people aged ≥ 60 years was 40.4%,[2] national-wide nutrition survey in 2002 showed the prevalence was 49.1%,[3] the results of a national-wide cross-sectional survey of hypertension using a multi-stage stratified random sampling method during 2012–2015 showed the prevalence of hypertension in people aged ≥ 60 years was 53.2%,[4] the prevalence of hypertension showed an increasing trend generally. Hypertension is significantly more common with the increase of age, a prevalence 51.5% in men and 55.3% in women.[2] The prevalence of hypertension rising more rapidly in rural areas than urban areas.[4]

The results of a survey conducted from 2012 to 2015 showed that the awareness rate, treated rate and controlled rate of hypertension in people aged over 60 years were 57.1%, 51.4% and 18.2%, respectively; which were significantly higher than those in 2002.[3] (Table 4). Compared by different demographic characteristics, the awareness rate, treated rate and controlled rate of women are higher than that of men, and the treated rate of hypertension in urban areas is significantly higher than that in rural areas.[5] Compared with northern areas of China, the awareness rate, treated rate and controlled rate of hypertension patients in southern areas are higher.[6,7] Compared with different ethnic groups, the treated rate and controlled rate of hypertension in ethnic minorities is lower than that in Han people.[8] Notably, the "three rate" of hypertension in Chinese population is still at a low level, and the controlled rate in elderly hypertensive patients has not been improved by the increased using of anti-hypertensive agents.[9]

1.4 The characteristics of hypertension in the elderly

With the increasing of age, the elasticity of large arteries decreased, and the stiffness increased; baroreceptor reflex sensitivity and beta-adrenergic system responsiveness decreased; the ability of the kidney to maintain the ion balance decreased. The capacity of neuro-hormonal regulation of BP in the elderly decreased, which was manifested by increased volume load and increased peripheral vascular resistance.[10]

High SBP and pulse pressure are common in elderly patients with hypertension. According to the statistics in China, the prevalence of isolated systolic hypertension in the elderly is 21.5%, accounting for 53.21% hypertensions in the elderly.[11] The incidence of calcified valvular disease increases with age, echocardiography can give a definite diagnosis. If the degree of aortic stenosis is more than 75%, the BP should not be over reduced, in case of perfusion of important organs being affected; if the pulse pressure is very high, SBP is significantly increased and DBP < 50 mmHg, aortic valve insufficiency should be suspected.

Because of the decline of BP regulation capacity, the BP level of the elderly can be easily affected by various factors, such as body position, eating, mood, season or temperature, which is called abnormal BP fluctuation. Postural hypotension, postprandial hypotension and abnormal circadian rhythm of BP are the most common.

The very old (≥ 80 years old) patients with hypertension are often accompanied with a variety of risk factors and related diseases. The rates of diabetes mellitus, hyper-

Table 4. Prevalence, awareness rate, treated rate, controlled rate, the results of two surveys in China.

Year	Age	Prevalence	Awareness rate	Treatment rate	Control rate
2002	≥ 60	49.1%	37.6%	32.2%	7.6%
2012–2015	≥ 60	53.2%	57.1%	51.4%	18.2%

lipidemia, coronary heart disease, kidney dysfunction and cerebrovascular disease are 39.8%, 51.6%, 52.7%, 19.9% and 48.4%, respectively.[12]

When elderly patients with hypertension are accompanied with severe arteriosclerosis, it is difficult to compress the brachial artery during the cuff inflation, the BP value is higher than the intra-arterial pressure value, and this phenomenon is called pseudo-hypertension.

Relatively accurate BP can be obtained by noninvasive central artery pressure measurement. The incidence of pseudo-hypertension increased with age.[13] Pseudo-hypertension should be considered when SBP is abnormally elevated without associated target organ damage (TOD) or with symptoms of hypotension developed after antihypertensive treatment. Pseudo-hypertension may cause over treatment of hypertension, and low SBP in elderly patients may lead to an unfavorable prognosis such as falls and frailty.[12]

2 Diagnosis and assessment

The diagnostic assessment of hypertension in the elderly includes: (1) confirm the BP level; (2) identify the cardiovascular risk factors; (3) identify the reversible and/or treatable factors causing hypertension, such as secondary hypertension; and (4) assess the hypertension mediated organ damage and related clinical conditions to determine the concomitant diseases that may affect prognosis. The assessment is particularly helpful to guide the treatment of the elderly hypertensive patients.

2.1 BP measurement

BP measurement is the basic mean and method to evaluate the BP level, diagnose hypertension and observe effect of the treatment. Because the elderly may have the characteristics of high BP fluctuation, nocturnal hypertension, morning hypertension and postural hypotension, it is necessary to encourage elderly hypertensive patients to take home BP measurement and ambulatory BP monitoring, and measure the BP of both upper limbs and low extremities regularly (such as every year) and BP in different positions (standing and lying position).[14] In particular, BP at certain time should be particularly noticed, such as BP before bedtime, during early morning period and before taking medicine.

2.1.1 Office BP measurement

Office BP measurement refers to the BP measurement carried out by the medical staff following the norms of BP measurement in the hospital environment. It is a common method to evaluate the BP level and observe the effect of the antihypertensive treatment.

2.1.2 Out-of-office BP measurement

Out-of-office BP measurement is more suitable for elderly patients with hypertension, more representative of daily life, and it may predict cardiovascular morbidity and mortality better than office BP.[15] Out-of-office BP measurement includes HBPM and ABPM.

HBPM, also called BP self-monitoring, can be used to evaluate BP control and long-term BP variability for days, weeks, months or even years, which are beneficial to treatment compliance. The measuring method[16,17] including: (1) it is recommended to use an upper arm automatic home-used electronic sphygmomanometer certified by the International Standard Scheme. It is not recommended to use wrist sphygmomanometer and finger sphygmomanometer or mercury sphygmomanometer for HBPM. The electronic sphygmomanometer should be calibrated regularly, at least once a year; (2) compared with office BP, HBPM values are usually lower, and the diagnostic threshold for hypertension is $\geq$ 135/85 mmHg (equivalent to office BP $\geq$ 140/90 mmHg); (3) when the treatment is just initiated, BP is unstable or the medication regimen is being adjusted, it is recommended to measure BP at every morning and evening (repeat for 2–3 times, calculate the average BP) for continuous seven days, calculate the average BP of the last six days. For those with stable BP, BP can be measured only one day in a week; for patients with long-term drug treatment, it is recommended to monitor the BP before the drug treatment, in order to evaluate the efficacy of the drug; (4) it is better to record the date and time of each BP measurement and all BP readings in detail, rather than average value only, so that doctors can instruct the BP monitoring and evaluate the efficacy of the treatment; and (5) HBPM is not recommended for patients with severe anxiety.

ABPM[18] is the BP level and the fluctuation of BP in daily work and life were continuously measured by automatic BP measuring instrument. Particularly, BP monitoring during night-time (sleep) may[19] provide comprehensive and accurate information about BP level and its fluctuation, help to identify the white coat hypertension, masked hypertension and isolated nocturnal hypertension.[20] The variability of BP in the elderly is large. The incidence of non-dipper BP can be as high as 69%.[21] The measuring method including: (1) the ambulatory BP monitor device should be certified by international standard scheme, and the device should be calibrated regularly; (2) BPs are typically recorded every 20 min during the day, and every 30 min during sleep at night. Valid BP monitoring should be ensured

throughout the 24 h period, with at least one BP reading per hour; the valid BP recordings should be more than 70% of all the recordings; and (3) parameters of ambulatory BP monitoring: 24 h, daytime (or awake), night- time (or sleep) mean SBP and mean DBP. The diagnostic threshold for hypertension is ≥ 130/80 mmHg over 24 h, ≥ 135/85 mmHg for the daytime average, and ≥ 120/70 mmHg for the night-time average. A number of additional value derived from ABPM recordings could be obtained, such as the degree of night-time BP dipping, BP level in the morning, 24 h BP variability, BP load, morning BP surge, Ambulatory Arterial Stiffness Index (AASI).

2.2 Medical history, physical examination and lab tests

For newly diagnosed elderly hypertensive patients, we should have a thorough understanding of their symptoms and medical history, including the following contents: (1) duration of hypertension, maximum BP, antihypertensive treatment and compliance; (2) past history: coronary heart disease, heart failure, cerebrovascular disease, kidney disease, peripheral vascular disease, diabetes mellitus, dyslipidemia, hyperuricemia, sleep apnea syndrome, thyroid dysfunction, rheumatoid arthritis and other diseases, treatment history; (3) family history: hypertension, coronary heart disease, stroke, kidney disease, diabetes and dyslipidemia; (4) clinical manifestations of secondary hypertension; (5) drugs being taken and adverse effects that have occurred; (6) lifestyle includes dietary fat, salt, alcohol, coffee intake, smoking time, the number of cigarettes smoked per day, change of body weight; and (7) psychosocial factors include family status, living environment and history of psychic trauma.

Careful physical examination is helpful to discover the clues of secondary hypertension and TOD: (1) measurement of body mass index (BMI), waist circumference and hip circumference; (2) observation of special facial features, centripetal obesity, skin purple lines, hairy and hyperthyroidism exophthalmos; (3) palpation of thyroid gland, presence or absence of renal enlargement (polycystic kidney) or mass; (4) auscultation of murmurs of carotid artery, thoracic aorta, abdomen artery and femoral artery; (5) thorough cardiopulmonary examination; (6) measurement of limb BP (at least both upper arms), arterial pulsation and nervous system signs; and (7) fundus endoscopy examination of retina abnormalities.

In addition to blood biochemistry (including fasting blood glucose, blood lipid, blood uric acid, liver and kidney function, and electrolytes especially blood potassium), blood routine, urine analysis and electrocardiogram, it is recommended for elderly patients to monitor fasting and postprandial blood glucose, to test glycosylated hemoglobin, urinary microalbumin quantification, 24 h urinary protein quantification (for protein-positive patients in urine routine test), and to monitor 24 h ambulatory BP, to take echocardiography. Further tests include carotid artery ultrasound, chest X-ray, fundus examination, pulse wave conduction velocity, ankle-arm BP index, and assessment of frailty of the elderly. The thickness of left ventricular wall increases with age, echocardiography is helpful to recognize the difference between physiological age-related left ventricular wall thickening and TOD caused by hypertension in the elderly.[22] For those suspected of secondary hypertension, relevant examinations should be considered.

2.3 Cardiovascular risk stratification

Although BP level is an important factor affecting the occurrence and prognosis of cardiovascular events, it is not the only factor. Therefore, a comprehensive and holistic assessment of cardiovascular risk in elderly patients with hypertension is needed.

2.3.1 Assessment of risk factors[23–26]

Risk factors include blood pressure (Grades 1–3), smoking or passive smoking, dyslipidemia (total cholesterol ≥ 5.2 mmol/L or low density lipoprotein cholesterol ≥ 3.4 mmol/L or high density lipoprotein cholesterol < 1.0 mmol/L), impaired glucose tolerance (2 h postprandial blood glucose 7.8–11.0 mmol/L) and (or) abnormal fasting blood glucose (6.1–6.9 mmol/L), abdominal obesity (waist circumference: male ≥ 90 cm, female ≥ 85 cm) or obesity (BMI ≥ 28 kg/m^2), family history of early-onset cardiovascular disease (the age of onset in first-degree relatives < 50 years), *etc.*.

Hypertension is the most important cardiovascular risk factor at present. High sodium diet, low potassium diet, overweight, obesity, alcohol consumption, mental stress and lack of physical activity are important risk factors for hypertension. Notably, old age is a risk factor for cardiovascular disease and hypertension.

Risk factors should be assessed regularly in both first-diagnosed hypertensive patients and patients on the treatment.

2.3.2 Screening for TOD[23]

Detection of asymptomatic subclinical TOD in hypertensive patients is an important part of the diagnosis and evaluation of hypertension. It includes left ventricular hypertrophy (interventricular septum or posterior wall thickness of left ventricle ≥ 11 mm or left ventricular mass index (LVMI): male ≥ 115 g/m^2, female ≥ 95 g/m^2, carotid intima-media thickness (≥ 0.9 mm) or plaque, carotid-femoral pulse wave velocity ≥ 12 m/s, ankle/arm index < 0.9, de-

creased estimated glomerular filtration rate [30–59 mL/(min·1.73 m^2)] or mild elevation of serum creatinine (115–133 μmol/L for male, 107–124 μmol/L for female) and microalbuminuria (30–300 mg/24 h or albumin/creatinine ratio 30–300 mg/g). A patient can have multiple TODs.

2.3.3 Concomitant diseases[23,26]

These concomitant diseases include heart disease (myocardial infarction, angina pectoris, coronary revascularization, and congestive heart failure), cerebrovascular disease (ischemic stroke, cerebral hemorrhage, and transient ischemic attack), diabetes, kidney disease (diabetic nephropathy, impaired renal function), and peripheral vascular disease.

2.3.4 Risk categories[20]

Assessing the overall risk of elderly patients with hypertension may help to determine when to initiate antihypertensive treatment, optimize treatment strategy and integrate cardiovascular risk management. Given that old age itself is a risk factor, elderly hypertensive patients are inevitably stratified to the middle-risk group or above. (Table 5).

2.4 Frailty assessment and preservation of cognitive function

2.4.1 Frailty assessment for elderly hypertension patients

Frailty is one of the manifestations of aging,[27,28] and its incidence increases significantly with age.[28] Several studies have found that frailty is one of the important factors affecting the benefits of antihypertensive therapy in the elderly.[30–34] Although the Hypertension in the Very Elderly Trial (HYVET) study subgroup analysis[35] and SPRINT study[36,37] showed that the elderly with frailty may benefit from intensive antihypertensive therapy, the impact of frailty on the prognosis and the goal of BP control still need further study, because the selected subjects were relative healthy and the health evaluation methods were inconsistent.

We can use several tools for frailty screening, FRAIL scale[43] proposed by the International Association of Geriatric Nutrition and Health, the gait speed measurement,[44] and the classical Fried criteria for frailty syndrome.[41,45,46] (Tables 7 & 8).

2.4.2 Hypertension in the elderly and cognitive dysfunction

Antihypertensive therapy may delay the age-related cognitive decline and reduce the risk of dementia. Both too high and too low blood pressure in the elderly may increase the risk of cognitive dysfunction.[48,49] For elderly patients with hypertension, cognitive function can be assessed at an early time, reasonable antihypertensive treatment and BP treatment target can be determined based on the biological age and cardiovascular risk stratification of the elderly.

Table 5. Risk categories of hypertension in elderly patients.

Other risk factors and medical history	Level of BP		
	Grade 1	Grade 2	Grade 3
1–2 risk factors	Moderate	Moderate	Very high
≥ 3 risk factors or TODs or diabetic mellitus	High	High	Very high
Concomitant clinical situation	Very high	Very high	Very high

BP: blood pressure; TODs: target organ damages.

Table 6. Recommendation for the frailty assessment of hypertension in the elderly.

Recommendation	Class	Level
Frailty should be assessed before the antihypertensive treatment for elderly hypertensive patients, in order to assess the benefits and risks of antihypertensive treatment,[38–40] especially in elderly hypertensive patients who lost more than 5% of their body weight during the past year without deliberate dieting or had a risk for falling.[41,42]	I	B

Table 7. FRAIL scale.[47]

No.	Items	Questions
1	Fatigue	You feel tired all or most of the time during the past four weeks.
2	Resistance	By yourself and not using aids, you have difficulty walking up one stair without resting.
3	Ambulation	By yourself and not using aids, you have difficulty walking one block or 100 m.
4	Illness	A doctor has told you that you have more than five illnesses. The illnesses include hypertension, diabetes, cancer (other than a micro-dermal carcinoma), chronic lung disease, heart attack, congestive heart failure, angina, asthma, arthritis, stroke, and kidney disease.
5	Loss of weight	Weight loss ≥ 5% occurs in one year or less.

Frail: ≥ 3 items; pre-frail: 1–3 items; robust: 0 item.

Table 8. Fried frailty assessment.[45]

No.	Items	Male	Female
1	Loss of weight	Unintentional weight loss [10 Ibs (4.5 kg) or > 5%] in past year	
2	Walking time, 4.57 m	Height ≤ 173 cm: ≥ 7 s	Height ≤ 159 cm: ≥ 7 s
		Height > 173 cm: ≥ 6 s	Height >159 cm: ≥ 6 s
3	Grip strength, kg	BMI ≤ 24.0 kg/m^2 ≤ 29	BMI ≤ 23.0 kg/m^2: ≤ 17
		BMI 24.1–26.0 kg/m^2: ≤ 30	BMI 23.1–26.0 kg/m^2: ≤ 17.3
		BMI 26.1–28.0 kg/m^2: ≤ 30	BMI 26.1–29.0 kg/m^2: ≤ 18
		BMI > 28.0 kg/m^2: ≤ 32	BMI > 29.0 kg/m^2: ≤ 21
4	Physical activity (MLTA)	< 383 kcal/week (walk about 2.5 h)	< 270 kcal/week (Walk about 2 h)
5	Exhaustion	Any item in CES-D scored 2–3. How many days have you experienced in the past week? (1) I felt that doing all the things need efforts. (2) I could not get going. Scored 0: < 1 d; Scored 1: 1–2 d; Scored 2: ≥ 3–4 d; Scored 3: < 4 d.	

Patients with 3–5, 1–2, and 0 factors are classified as frail, pre-frail, and robust, respectively. BMI: body mass index; CES-D: Center for Epidemiologic Studies-Depression questionnaire; MLTA: Minnesota leisure time activity.

3 Treatment

3.1 Introduction

3.1.1 Objective of antihypertensive therapy

The objectives of antihypertensive therapy include reducing the development of cardiovascular disease caused by hypertension, reducing the morbidity and mortality of cardiovascular disease to the greatest extent, and improving the quality of life and prolonging life span.[23] Achieving the SBP target should be emphasized in the treatment of hypertension in the elderly. If tolerated, BP target should be achieved gradually. After initiation of antihypertensive therapy, BP should be monitored to avoid adverse effects caused by sharp decline of the BP.

3.1.2 Integrated therapy of cardiovascular risk factors

While pursuing the BP target, all reversible cardiovascular risk factors (such as smoking, dyslipidemia or obesity, abnormal blood glucose metabolism or elevated uric acid, *etc.*) should be intervened. Meanwhile, relevant TOD and concomitant diseases should be concerned and treated.[50] Most patients need long-term or even lifelong treatment.

3.1.3 Recommendations for BP thresholds for treatment and targets of BP

Elderly patients with hypertension have a higher cardiovascular risk, those patients may benefit more from strict BP control.[51] (Table 9).

3.2 Non-pharmacological therapy for hypertension

Non-pharmacological treatment is the basis of antihypertensive therapy. It is recommended that healthy lifestyle should be maintained regardless drug treatment, including healthy diet, regular physical activity, smoking cessation, alcohol restriction, maintaining ideal weight, improving sleep and keeping warm.

3.2.1 Healthy diet

Sodium restrict and potassium-rich diet may help the patients control the BP.[58–62] WHO recommends that daily salt

Table 9. Recommendation for BP thresholds for treatment and targets of BP.

Recommendation	Class	Level
Initiation of BP-lowering drug treatment is recommended for patients aged ≥ 65 years and BP ≥ 140/90 mmHg, simultaneous with the initiation of lifestyle changes,[52,53] the target is < 140/90 mmHg.[54,55]	I	A
Initiation of BP-lowering drug treatment should be considered for patients aged ≥ 80 years and BP ≥ 150/90 mmHg,[54] the first goal should be lowering BP to < 150/90 mmHg. Provided that the treatment is well tolerated, BP target should be 140/90 mmHg or lower.[51,56]	IIa	B
If the very old patients with hypertension are classified as frail, BP ≥ 160/90 mmHg, the drug treatment should be initiated, SBP values should be targeted to 150 mmHg or lower, but ≥ 130 mmHg as possible.	IIa	C
Discontinuing treatment if the treatment is well tolerated is not recommended.[57]	III	A

BP: blood pressure; SBP: systolic blood pressure.

intake should be less than 6 g, and moderate salt restriction should be applied to elderly patients with hypertension. Elderly people are encouraged to eat varieties of fresh vegetables, fruits, fish, bean products, coarse grains, skim milk and other foods rich in potassium, calcium, dietary fiber and polyunsaturated fatty acids.

3.2.2 Regular physical activity

Appropriate aerobic physical activity can effectively reduce BP in elderly patients with hypertension and pre-hypertension.[63,64] It is suggested that the elderly should take appropriate physical activity regularly, no less than five days a week and no less than 30 min of aerobic physical activity per day. The recommended activities include walking, jogging and swimming. Vigorous exercise is not recommended for the elderly.

3.2.3 Smoking cessation and alcohol restriction

Smoking cessation reduces the risk of cardiovascular and pulmonary diseases.[65,66] Elderly people should limit alcohol intake, men should drink less than 25 g of alcohol per day and women should drink less than 15 g of alcohol per day. Liquor, wine (or rice wine) or beer consumption should be less than 50 mL, 100 mL and 300 mL, respectively.

3.2.4 Maintain an ideal body weight

Overweight or obese elderly patients with hypertension should restrict calories intake and do more physical activities.[67] Maintaining ideal body weight (BMI: 20.0–23.9 kg/m^2) and rectifying abdominal obesity (male abdominal circumference ≥ 90 cm, female abdominal circumference ≥ 85 cm) are beneficial to controlling BP and reducing the risk of cardiovascular disease, but the elderly should avoid rapid or excessive weight loss.

3.2.5 Sleep improvement

Duration and quality of sleep are associated with elevated BP and cardiovascular risk.[68] Ensuring adequate sleep and improving sleep quality are of great significance for improving quality of life, controlling BP and reducing complications of cardiovascular and cerebrovascular diseases.

3.2.6 Keep warm

BP changes with seasons.[69] The cold tolerance and capacity of BP regulation is poor in the elderly. BP often fluctuates seasonally. We should keep the room warm and ventilate regularly; reduce outdoor activities when the temperature decline sharply with the strong wind; add clothes appropriately to avoid large fluctuations of BP.

3.3 Pharmacological therapy for hypertension

3.3.1 Basic principles of pharmacological therapy for the elderly

The following principles should be followed when we treat elderly patients with hypertension: (1) low dose: initial treatment usually adopts a lower effective dose, and then increases the dose gradually as needed; (2) long-acting drugs: as far as possible, we should use long-acting and 24 h effective antihypertensive drugs that could be administrated once a day to control BP effectively during night and morning; (3) combination of drugs: if the therapeutic effect of single drug is unsatisfactory, two or more types low-dose antihypertensive drugs can be used to increase the antihypertensive effect. Single pill combinations may help to improve the patient compliance; (4) using drugs reasonably: most elderly patients need combined antihypertensive therapy, even at the initial stage. Initial combined therapy is not recommended for frail elderly and older people aged over 80 years; and (5) individualized treatment: to select appropriate antihypertensive drugs for the patients according to the specific conditions, tolerance, personal willingness and economic status.

3.3.2 Types and characteristics of commonly used antihypertensive drugs

Commonly used antihypertensive drugs include: Calcium Channel Blockers (CCB), Angiotensin Converting Enzyme Inhibitor (ACEI), Angiotensin Receptor Blocker (ARB), diuretics, β-blockers. Other types of antihypertensive drugs may sometimes be used in certain populations. (Table 10).

CCB, ACEI, ARB, diuretics and fixed-dose single-pill combinations can be used as an initial or long-term maintenance treatment of hypertension in the elderly.[70–79] Taking the risk factors, subclinical TOD and concomitant clinical diseases of patients into consideration a certain type of antihypertensive drug is preferred.[80–83] (Tables 11 & 12). The detail information of antihypertensive drugs include the following:

(1) Diuretics. Thiazide diuretics are the most common diuretics. They belong to the medium-effect diuretics. They can be classified as thiazide diuretics (such as hydrochlorothiazide) or thiazide-like diuretics (such as indapamide) based on their molecular structure. Potassium-sparing diuretics belong to the low-effect diuretics, which can be classified into two categories. Aldosterone receptor antagonist, the representative drugs including spironolactone and eplerenone. Pharmacological effects of another type do not depend on aldosterone. The representative drugs include triamterene and amiloride. Diuretics are especially suitable for elderly

Table 10. Commonly used antihypertensive drugs.

Types	Drugs	Daily dose, mg/d	Times per day	Precautions
Thiazide/Thiazide-like diuretics	Chlorthalidone	6.25–25	1	Sodium, potassium, uric acid and calcium concentrations should be monitored.
	Indapamide	0.625–2.5	1	Use cautiously if the patient has a history of gout, unless the patient has received uric acid lowering therapy.
Loop diuretics	Bumetanide	0.5–4	2	For patients with symptomatic heart failure, loop diuretics are preferred.
	Furosemide	20–80	1–2	For patients with CKD stage 3–4, loop diuretics are preferred.
	Torasemide	5–10	1	
Potassium-sparing diuretics	Amiloride	5–10	1–2	The antihypertensive effect of single use was not obvious.
	Triamterene	25–100	1–2	Avoid these drugs in patients with CKD stage 5.
Aldosterone antagonists	Eplerenone	50–100	1–2	Spironolactone increases the risk of breast hyperplasia and ED in men compared with eplerenone.
	Spironolactone	20–60	1–3	Avoid the combination with potassium supplements and potassium sparing drugs. Avoid these drugs in patients with CKD stage 3–4.
CCB (Dihydropyridine)	Amlodipine besylate	2.5–10	1	
	Levamlodipine maleate	1.25–5	1	
	Levamlodipine besylate	1.25–5	1	
	Felodipine	2.5–10	1	No absolute contraindication.
	Lercanidipine	10–20	1	Dose-related ankle edema, flushing and constipation were more common in females than in males.
	Nifedipine delayed-release tablets	10–80	2	
	Nifedipine controlled released tablets	30–60	1	The side effects of levamlodipine like ankle edema were relatively few.
	Lacidipine	4–8	1	
	Cinidipine	5–10	1	
	Benidipine	4–8	1	
CCB (Non-dihydropyridine)	Diltiazem	90–180	2–3	
	Diltiazem sustained release tablets	90–360	1–2	Avoid routine combination with beta blockers for the potential of bradycardia and conduction block.
	Verapamil sustained release tablets	120–240	1–2	Not suitable for systolic heart failure.
ACEI	Benazepril	5–40	1–2	The combination of ACEI and ARB is not recommended.
	Captopril	25–300	2–3	
	Enalapril	2.5–40	1–2	Patients with CKD or using potassium supplements or potassium-preserving drugs increase the risk of high potassium.
	Fosinopril	10–40	1	
	Lisinopril	2.5–40	1	Risk of acute renal failure increased in patients with severe bilateral renal artery stenosis.
	Imidapril	2.5–10	1	The ACEI are contraindicated in patients with previous angioedema associated with ACE inhibitor therapy.
	Perindopril	4–8	1	
	Ramipril	1.25–20	1	The ACEI are contraindicated in patients with serum creatinine > 3 mg/dL.
ARB	Candesartan	4–32	1	
	Irbesartan	150–300	1	
	Losartan	25–100	1	Indications and contraindications as same as ACEI.
	Olmesartan	20–40	1	The combination of ACEI and ARB is not recommended.
	Telmisartan	20–80	1	ARB is an altered choice for patients with dry cough who cannot tolerate ACEI.
	Valsartan	80–160	1	
	Allisartan	240	1	
Cardio-selective beta blockers	Atenolol	12.5–50	1–2	
	Bisoprolol	2.5–10	1	β-blockers are contraindicated in patients with disease of bronchospasm.
	Metoprolol tartrate	25–100	2	When β-blockers must be used, highly β1-selective beta blockers could be selected. Avoid abrupt withdrawal.
	Metoprolol succinate	23.75–190	1	
Non-selective beta blockers (mixed Alpha + Beta blockers)	Carvedilol	12.5–50	2	Beta blockers are contraindicated in patients with disease of bronchospasm.
	Aronixil	10–20	1–2	When beta blockers must be used, highly β1-selective beta blockers could be selected.
	Labetalol	200–600	2	Avoid abrupt withdrawal.
α1-receptor antagonism	Doxazosin	1–16	1	Those drugs may cause postural hypotension, particularly in the elderly patients.
	Prazosin	1–10	2–3	α1-receptor antagonism can be used as second-line drug for the patients with benign prostatic hyperplasia.
	Terazosin	1–20	1–2	
Centrally active drugs	Clonidine	0.1–0.8	2–3	
	Methyldopa	250–1000	2–3	Avoid abrupt withdrawal in case of hypertensive crisis.
	Reserpine	0.05–0.25	1	
Direct vasodilator	Hydralazine	25–100	2	High dose may cause hirsutism and lupus syndrome.

ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; CKD: chronic kidney disease; ED: erectile dysfunction.

Table 11. Preferred drugs in certain clinical condition.

Clinical conditions	Drugs
Asymptomatic TOD	
LVH	ACEI, CCB, ARB
Asymptomatic atherosclerosis	ACEI, CCB, ARB
Microalbuminuria	ACEI, ARB
Mild renal insufficiency	ACEI, ARB
Clinical cardiovascular events	
Previous myocardial infarction	BB, ACEI, ARB
Angina pectoris	BB, CCB
Heart failure	Diuretics, BB, ACEI, ARB, Aldosterone antagonist
Aortic aneurysm	BB
AF, prevention	ACEI, ARB, BB, Aldosterone antagonist
AF, ventricular rate control	BB, non-dihydropyridine CCB
Peripheral arterial diseases	ACEI, CCB, ARB
Other	
Isolated systolic hypertension (elderly)	Diuretics, CCB
Metabolic syndrome	ACEI, ARB, CCB
Diabetes	ACEI, ARB

ACEI: angiotensin-converting-enzyme inhibitor; AF: atrial fibrillation; ARB: Angiotensin receptor blocker; BB: β-blocker; CCB: Calcium channel blocker; LVH: left ventricular hypertrophy; TOD: target organ damage.

Table 12. Selection of antihypertensive dugs for the elderly patients.

Recommendation	Class	Level
Thiazide/thiazide-like diuretics, CCB, ACEI and ARB are recommended for the initiation and maintenance of antihypertension therapy.[56,82,83,85,86]	I	A
For most elderly patients with more than 20 mmHg above the target BP, a combination of two drugs is recommended as the initial treatment.[95,97]	I	A
If the BP target is still not achieved, the combination of thiazide/ thiazide-like diuretic, CCB and ACEI/ARB is recommended, or single-pill combination is also recommended.[98,99]	I	A
Drug therapy for very old patients aged over 80 years and frail elderly patients is recommended start with low dose monotherapy.[54–56]	I	A
The combination of two RAS inhibitor is not recommended.[56,82–85,88,90–92]	III	A

ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; RAS: renin-angiotensin system.

patients with hypertension, resistant hypertension, heart failure with hypertension and sodium-sensitive hypertension. Small dose of diuretics are recommended for single drug therapy to avoid adverse effects.

Post-stroke antihypertensive treatment study (PATS) was conducted by Chinese independently. It is the first large-scale placebo-controlled clinical trial of post-stroke antihypertensive therapy as a secondary prevention in the world. The results showed that the BP of indapamide (2.5 mg/d) treatment group is 5/2 mmHg lower than that of placebo group, and the incidence of stroke was reduced by 29%.[84] The results of HYVET showed that if the SBP was reduced to 150 mmHg by 1.5 mg/d of sustained-release indapamide in elderly patients with SBP above 160 mmHg (≥ 80 years old), compared with placebo, the risks of stroke and death are reduced by 34% and 28%, respectively.[56]

(2) CCB. Based on the different affinity and effectiveness to the blood vessel and heart, it can be classified into dihydropyridine CCB and non-dihydropyridine CCB. Different CCBs have different durations of effect, vascular selectivity, pharmacokinetics, antihypertensive effects and adverse effects.

Systolic Hypertension in China (Syst-China) clinical trial[85] and Shanghai trial of nifedipine in the elderly (STONE)[86] confirmed that CCB-based antihypertensive therapy, such as nitrendipine and nifedipine, could significantly reduce the incidence and mortality of stroke of the hypertensive patients in China. International Nifedipine GITS study (INSIGHT Study) confirmed that nifedipine controlled release tablets could significantly reduce the risk

of cardiovascular and cerebrovascular events.[87] Felodipine Event Reduction study (FEVER) showed that compared with hydrochlorothiazide alone, combination of hydrochlorothiazide with felodipine could further reduce BP by 4/2 mmHg and reduce fatal and non-fatal stroke by 27%. FEVER post-analysis showed that stroke, cardiac events and total mortality risk were the lowest when the average BP level was below 120/70 mmHg after treatment.[88] LEADER study, one of the national "Twelfth Five-Year Plan" projects, showed that levamlodipine maleate could effectively reduce the cardio- cerebrovascular composite endpoint events in the patients with hypertension in China. The incidence of lower limb edema and other adverse effects was lower compared with amlodipine.[89]

(3) ACEI. The mechanism of different ACEI preparations is similar. ACEI has a favorable effect on target organ protection and cardiovascular endpoint event prevention, especially for the elderly hypertensive patients with chronic heart failure and myocardial infarction. ACEI has no unfavorable effects on glucose and lipid metabolism, it can effectively reduce urinary albumin excretion and delay the progression of renal diseases. It is suitable for elderly hypertensive patients with diabetic nephropathy, metabolic syndrome, chronic kidney disease (CKD), proteinuria or microalbuminuria.[81]

The Perindopril Protection against Recurrent Stroke Study (PROGRESS), an international cooperative study, in which China has participated, selected about 1/4 of 6105 patients in the whole trial. The results showed that perindopril plus indapamide or single drug therapy reduced the risk of stroke recurrence by 28% overall. The combined treatment of perindopril and indapamide had better antihypertensive effect than perindopril alone. Subgroup analysis showed that Asian subjects such as Chinese and Japanese had a greater reduction in stroke risk. The 6-year follow-up data of 1520 selected patients in China confirmed that antihypertensive therapy significantly reduced the risk of stroke recurrence, and the total mortality and the risk of myocardial infarction also showed a trend of decline.[90,91]

Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation study (ADVANCE), in which China has participated, selected approximately 30% study patients. The results showed that low-dose perindopril/indapamide compound reduced the combined end-point events of macrovascular and microvascular by 9% compared with conventional antihypertensive therapy in the treatment of diabetes mellitus patients.[92]

(4) ARB. ARB could reduce the risk of cardiovascular death, myocardial infarction, stroke or hospitalization due to heart failure in patients with high risk of cardiovascular events. ARB could reduce albuminuria and microalbuminuria in patients with diabetes or nephropathy[82,83] especially in patients with left ventricular hypertrophy, heart failure, diabetic nephropathy, metabolic syndrome, microalbuminuria or albuminuria and those who cannot tolerate ACEI.

(5) Beta blocker. Beta blockers can be applied for elderly hypertensive patients with tachyarrhythmia, angina pectoris and chronic heart failure. In comparison with other antihypertensive drugs, beta blockers did not show an advantage in reducing the incidence of stroke.[93,94] Therefore, beta blockers are not recommended for elderly patients with isolated systolic hypertension and stroke unless there are strong indications for beta blockers, such as coronary heart disease and heart failure.

3.3.3 Drug combinations for hypertension treatment

For elderly patients with hypertension whose BP target is not achieved using monotherapy, combination of two antihypertensive drugs can be used.[53,88,100–103] Combination therapy may start with low-dose regimen. If BP is not well controlled, it can be gradually adjusted to the standard dose. The mechanisms of different antihypertensive drugs may be complementary to each other, different drugs may counteract or alleviate the adverse effects of each other, for example, ACEI or ARB combined with low dose thiazide diuretics. The combination of ACEI and ARB[104,105] should be avoided. However, thiazide diuretics or loop diuretics and potassium- preserving diuretics can be used in combination under certain conditions (e.g., hypertension with heart failure); so could dihydropyridine CCB and non-dihydropyridine CCB.

The combination of dihydropyridine calcium channel blocker + ACEI (or ARB) + thiazide diuretics is most commonly used when the combination of three drugs is needed. For patients with resistant hypertension, a fourth drug, such as aldosterone antagonists, beta-blocker or alpha-blocker, could be added.

Fixed-dosed single-pill combination antihypertensive agents usually contain drugs with different pharmacological mechanisms. Single-pill combination agents are more convenient in comparison with administration respectively, thus compliance in elderly patients may be improved.[106] Most of the fixed-dosed single-pill combination agents currently used in China include ACEI + thiazide diuretics, ARB + thiazide diuretics, dihydropyridine calcium channel blockers + ARB, dihydropyridine calcium channel blockers + beta blockers, thiazide diuretics + potassium-preserving diuretics.

Reserpine triamterene tablet (Antihypertension No.0), is also widely used in China. Reserpine triamterene tablet mainly consist hydrochlorothiazide, triamterene, dihydralazine sulfate and reserpine. This drug is economic, with satisfactory antihypertensive effect according with the basic principle of

antihypertensive drugs in the elderly and good synergistic effect with ACEI (or ARB), CCB and other antihypertensive drugs, so it is still an option for hypertensive patients.[107–109]

3.3.4 Follow-up of antihypertensive therapy

Appropriate follow-up and monitoring could assess the treatment compliance and responsiveness, it may help achieve the target BP, detect adverse effects and TOD.[110,111] After initiating new drugs therapy or adjustment of the treatment, compliance and treatment response need to be evaluated monthly until the BP target is achieved. Follow-up should include much information, such as BP level, postural hypotension, adverse drug effects, treatment compliance, lifestyle changes, and the necessity of drug adjustment. Laboratory tests include electrolyte, renal function and other TOD.[110–112] After the initiation of antihypertensive drugs therapy, the application of home BP measurements, team care and appropriate telemedicine may help to improve the BP controlled rate of elderly patients.[113–118]

3.4 Hypertension in specific clinical conditions of the elderly

3.4.1 Hypertension in very old patient

For very old patients (age ≥ 80 years) with hypertension, the goal of antihypertensive therapy is to maintain organ function, to improve life quality, and to reduce the overall mortality[54,56] by a stratified and step-by-step treatment strategy. The selection of antihypertensive drugs should follow several principles: (1) initiate treatment with monotherapy; (2) preferred drugs should be stable, effective, safe, less adverse effects, simple administration, and good compliance, such as diuretics, controlled release CCB, ACEI or ARB; (3) if the monotherapy is not effective enough, it is recommended to initiate the combination therapy at the lowest effective doses; (4) be aware of risks and drug adverse effects caused by combination therapy; and (5) it is recommended to monitor the BP (include orthostatic BP) carefully, assess drug tolerance. If the symptoms of impaired perfusion come out, the intensity of the therapy should be lowered.

The antihypertensive therapy of the very old patients with hypertension should follow the step-by-step strategy. The therapy should be initiated when BP ≥ 150/90 mmHg. First, the BP should be lowered to < 150/90 mmHg, and if tolerated, the SBP could be further reduced to less than 140 mmHg.

3.4.2 Hypertension with cerebrovascular disease

The treatment strategies for elderly hypertensive patients with cerebrovascular disease see the Table 13 below.

3.4.3 Hypertension with coronary heart disease

Individualized and graded treatment strategies should be adopted for hypertensive patients with coronary heart disease. Antihypertensive drugs should be initiated at a low dose, increase the dose or add more drugs types gradually, achieve the BP target gradually. If angina pectoris symptoms related to antihypertensive therapy occur, the dosage of antihypertensive drugs should be reduced and possible inducements should be assessed. The treatment strategies for elderly hypertensive patients with coronary artery disease see the Table 14 below.

For patients with stable angina pectoris and/or previous history of myocardial infarction, beta blockers and renin-angiotensin system (RAS) inhibitors are preferred for initial antihypertensive therapy. Long-acting dihydropyridine CCB can be added when BP is difficult to control and angina persists. If no angina persists, dihydropyridine CCB, thiazide diuretics and/or aldosterone receptor antagonists can be selected. CCB is the first choice for patients with variant angina pectoris. Long-acting dihydropyridine CCB can also be used as an initial treatment for patients with stable angina pectoris without a history of myocardial infarction and heart failure. Initial antihypertensive therapy should include β- blockers and RAS inhibitors in patients with ACS without contraindications. If there is severe hypertension or persistent myocardial ischemia, intravenous beta-blockers

Table 13. Treatment strategies for elderly hypertensive patients with cerebrovascular disease.

Recommendation	Class	Level
For patients with acute cerebral hemorrhage, SBP should be lowered to < 180 mmHg.[119,120]	Ⅱa	B
In patients with acute ischemic stroke, lowering BP to < 200 mmHg is reasonable.	Ⅱa	C
In order to prevent recurrence of stroke and other vascular events, patients with acute ischemic stroke or TIA who had been treated with antihypertensive drugs for a long time in the past are recommended to resume antihypertensive therapy several days after the onset of the event.[91,121]	Ⅰ	A
The BP target of patients with history of ischemic stroke or TIA should be determined considering the specific circumstances. It is reasonable that BP should be lowered below 140/90 mmHg.[91,121]	Ⅱa	B
It is reasonable to lower the BP below 150/90 mmHg in elderly patients.	Ⅱa	C

BP: blood pressure; SBP: systolic blood pressure; TIA: transient ischemic attack.

Table 14. Treatment strategies for elderly hypertensive patients with coronary artery disease.

Recommendation	Class	Level
For patients aged < 80 years, it is recommended to target BP to < 140/90 mmHg.[122,123]	Ⅰ	A
If the body condition is good and the patient could tolerate the antihypertensive therapy, especially for those with previous myocardial infarction, the BP can be lowered to < 130/80 mmHg.[55]	Ⅱa	B
For patients aged ≥ 80 years, the target of BP should be < 150/90 mmHg. If tolerated, the BP should be further lowered to less than 140/90 mmHg.[56]	Ⅱa	B
For those with increased pulse pressure (≥ 60 mmHg), it is emphasized that the SBP should achieve the target value. When DBP < 60 mmHg, SBP should be lowered to target value gradually with carefully monitoring.	Ⅱa	C

BP: blood pressure; SBP: systolic blood pressure.

(esmolol, *etc.*) can be used. If BP is difficult to control or beta blockers are contraindicated, long-acting dihydropyridine CCB could be a choice; when there is evidence of heart failure or pulmonary congestion, non-dihydropyridine CCB should not be given. Nitrates can be used to control BP and relieve symptoms of myocardial ischemia and pulmonary congestion. If accompanied by myocardial infarction, heart failure or diabetes mellitus and poor BP control, aldosterone receptor antagonists could be added.

3.4.4 Hypertension with heart failure

Heart failure is a common concomitant disease of hypertension.[124] Regardless of ejection fraction, reasonable control of BP may help alleviate symptoms of heart failure and delay further deterioration of cardiac function. The therapeutic strategies for treatment of hypertension with the elderly with heart failure see the Table 15 below.

3.4.5 Hypertension with chronic kidney disease

The prevalence of hypertension in elderly patients with CKD increases with age, while the control rate of BP decreases gradually.[125–129] Tight BP control is one of the important means to reduce cardiovascular events and mortality in elderly patients with CKD effectively. The treatment strategies for elderly hypertensive patients with CKD see the Table 16 below. CKD stage in elderly people is the same as the general population. CKD stage 1: GFR ≥ 90 mL · min^{-1} · 1.73 m^{-2}; CKD stage 2: 60 ≤ GFR < 90 mL · min^{-1} · 1.73 m^{-2}; CKD stage 3: 30 ≤ GFR < 60 mL · min^{-1}· 1.73 m^{-2}; CKD stage 4: 15 ≤ GFR < 30 mL · min^{-1} · 1.73 m^{-2}; CKD stage 5: GFR < 15 mL · min^{-1} · 1.73 m^{-2}.

The recommendations for the selection of antihypertensive drugs see the Table 17 below.

3.4.6 Hypertension with diabetes mellitus

Hypertension and diabetes are both independent risk factors of cardiovascular and cerebrovascular diseases. When they coexist, the risk of cardiovascular and cerebrovascular diseases can be significantly increased.[141,142] Elderly diabetic patients are more likely to have hypertension,[143] and antihypertensive therapy can effectively reduce the incidence of atherosclerotic cardiovascular events, heart failure and microvascular complications in diabetic patients.[144,145]

The ACCORD study showed that for hypertensive patients with diabetes mellitus, too strict SBP control (< 120

Table 15. Therapeutic strategies for treatment of hypertension with the elderly with heart failure.

Recommendation	Class	Level
In elderly hypertensive patients with heart failure, BP should be controlled at < 140/90 mmHg first and further lowered to < 130/80 mmHg.[54,123,130]	Ⅱa	B
If there is no contraindications, ACEI or ARB, aldosterone antagonist, diuretics, beta blockers, angiotensin receptor enkephalin inhibitor are recommended .[51,131,132]	Ⅰ	A
Non-dihydropyridine calcium channel blockers (verapamil and diltiazem) are not recommended.	Ⅲ	C

ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; BP: blood pressure.

Table 16. Treatment strategies for elderly hypertensive patients with CKD.

Recommendation	Class	Level
The BP in elderly patients with CKD is recommended to be lowered to < 140/90 mmHg.[54,133]	Ⅰ	A
If the urinary protein is 30–300 mg/d or more, BP is recommended to be reduced to < 130/80 mmHg.[51,134,135]	Ⅰ	C
The SBP of hemodialysis patients should be less than 160 mmHg before dialysis, and the target of BP in elderly peritoneal dialysis patients can be extended to < 150/90 mmHg.[136–138]	Ⅱa	C

BP: blood pressure; CKD: chronic kidney disease; SBP: systolic blood pressure.

Table 17. Recommendation of antihypertensive drugs for elderly hypertensive patients with CKD.

Recommendation	Class	Level
ACEI or ARB is recommended for CKD patients, especially for patients with proteinuria.[138]	Ⅰ	A
Initiating at a low dose, ACEI or ARB may be used to the maximum dose[137] for hypertensive patients with diabetic nephropathy if tolerated.	Ⅱb	C
When ACEI or ARB is used, the initial dose of CKD3–4 patients should be reduced by half. Serum potassium and creatinine levels as well as eGFR should be carefully monitored. The dosage as well as the form of drugs should be adjusted in time.	Ⅱa	C
It is not recommended that ACEI/ARB be used together.[139]	Ⅲ	A
CCB is recommended for hypertensive patients with obvious renal dysfunction and salt sensitivity.[140]	Ⅰ	C
For CKD patients with volume overload, loop diuretics (such as furosemide) are recommended for CKD4 or CKD5.	Ⅰ	C
Alpha/beta receptor blockers may be considered to be used in combination antihypertensive therapy for patients with resistant hypertension and are not easily cleared by dialysis.	Ⅱb	C

ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate.

mmHg) did not reduce the incidence of fatal and non-fatal cardiovascular events. Therefore, comprehensive evaluation (comorbidity, cognitive and functional evaluation) should be carried out for elderly diabetic patients.[145] The treatment strategies for elderly hypertensive patients with diabetes mellitus see the Table 18 below.

The recommendation of antihypertensive drugs for elderly hypertensive patients with diabetes mellitus are listed in Table 19.

3.4.7 The management of resistant hypertension

Resistant hypertension (RH) is defined as the failure to reduce BP to < 140/90 mmHg in a month after taking a three-drug regimen (including diuretics) and improvement of life style or BP < 140/90 mmHg but patients require ≥ 4 antihypertensive medications.[159]

Pseudo-RH should be excluded firstly in the diagnosis of RH in the elderly. The causes of pseudo-RH including incorrect BP measurement, poor treatment compliance (patients did not adhere to medication), white coat hypertension and pseudo-hypertension.[160]

For patients who meet the diagnostic criteria of RH, we should find out the causes of poor BP control, the causes include: (1) inappropriate lifestyle: obesity, excessive drinking and high-salt diet; (2) the use of anti-hypertensive drugs inhibitor: non-steroidal anti-inflammatory drugs, steroids,

Table 18. Treatment strategies for elderly hypertensive patients with diabetes mellitus.

Recommendation	Class	Level
The BP of elderly diabetic patients is recommended to be controlled < 140/90 mmHg, if tolerated, the target is recommended to be < 130/80 mmHg.[144,147]	Ⅰ	A
DBP is recommended to be no less than 70 mmHg.	Ⅰ	C

BP: blood pressure; DBP: diastolic blood pressure.

Table 19. Recommendation of antihypertensive drugs for elderly hypertensive patients with diabetes mellitus.

Recommendation	Class	Level
ACEI/ARB is the first choice for patients with hypertension and diabetes mellitus. When ACEI is intolerable, ARB is recommended.[148,149]	Ⅰ	A
If the patients have diabetic nephropathy, especially those with UACR > 300 mg/g or eGFR < 60 mL · min^{-1} · (1.73 m^2)$^{-1}$, ACEI[150]/ARB[151,152], or as part of the combination therapy, is recommended.	Ⅰ	A
Dihydropyridine CCBs combined with ACEI or ARB are recommended for diabetic patients.[153,154]	Ⅰ	B
Loop diuretics[155] may be considered for diabetic patients with eGFR < 30 mL · min^{-1} ·1.73 · m^{-2}.	Ⅱb	C
Large dose of diuretics is not recommended.	Ⅲ	C
Beta blocker is not the first choice for diabetes mellitus patients. When necessary, low dose and hyper-selective beta1 blocker combined with ACEI or ARB may be considered.[156]	Ⅱb	C
The combination of beta blockers and diuretics is not recommended .[157]	Ⅲ	C
Elderly patients with prostatic hypertrophy may consider the use of alpha blockers, but the risk of orthostatic hypotension may be considered.[158]	Ⅱb	C

ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; UACR: urinary albumin-to-creatinine ratio.

Table 20. Treatment strategies for elderly patients with resistant hypertension.

Recommendation	Class	Level
It is recommended to eliminate factors affecting BP control, actively improve lifestyle and improve compliance.[166]	Ⅰ	B
If the target BP is not achieved, aldosterone antagonists should be considered. [167]	Ⅱa	B
β-blocker is recommended in patients with coronary heart disease or heart failure if the resting heart rate is high.[168,169]	Ⅰ	A
Alpha-1 beta receptor blockers[168,169] should be considered in elderly male patients with prostatic hyperplasia.	Ⅱa	B
Adding direct vasodilators (such as hydralazine, minoxidil) or central antihypertensive drugs (such as clonidine and alpha-methyldopa) may be considered for elderly patients with resistant hypertension. [170,171]	Ⅱb	B

BP: blood pressure; GFR: glomerular filtration rate.

erythropoietin, ephedrine, liquorice and antidepressants;[161–165] (3) inadequate drug treatment: inadequate dosage, absence of diuretics, inappropriate combination therapy; and (4) other factors: such as insomnia, prostatic hypertrophy (nocturnal urination often affects sleep), chronic pain and long-term anxiety, secondary hypertension. Treatment strategies for elderly patients with resistant hypertension are illustrated in the following Table 20.

The efficacy and safety of device-based hypertension treatment, such as percutaneous radiofrequency catheter ablation of renal sympathetic nerve and carotid sinus baroreceptor stimulation[172,173] in the elderly are not yet clear.[172,174–176]

3.4.8 Hypertension urgencies and emergencies

Hypertension emergencies are situations in which BP increases suddenly and significantly (generally more than 180/120 mmHg) under certain inducements in patients with primary or secondary hypertension, accompanied by acute progressive heart, brain, kidney and other important target organ dysfunction.[23] Hypertensive emergencies in the elderly mainly include hypertensive encephalopathy, intracranial hemorrhage (intracerebral hemorrhage and subarachnoid hemorrhage), cerebral infarction, acute heart failure, acute coronary syndrome, aortic dissection, kidney damage, severe perioperative hypertension, pheochromocytoma crisis, *etc*. Hypertension urgencies refer to a marked increase in BP without acute TOD. Patients may have symptoms caused by a significant increase in BP, such as headache, chest tightness, epistaxis and fidgety.[23] The degree of BP rising is not the differentia between hypertension emergencies and hypertension urgencies. It is the only differentia that whether there is newly-onset acute progressive severe TOD.

First target BP level of antihypertensive treatment in elderly hypertensive emergencies: reduce BP to a safe level within 30–60 min, except for stroke and aortic dissection. It is recommended that the mean arterial pressure should be reduced rapidly within 1–2 h, but not more than 25%. Second goal of antihypertensive therapy: after reaching the first target level, we should slow down the pace of BP lowering, add oral antihypertensive drugs, and reduce the intravenous drug delivery gradually. It is recommended that BP should be reduced to 160/100–110 mmHg within the next 2–6 h. The third goal of antihypertensive therapy: if the BP level of the second goal is tolerable and the clinical condition is stable, reduce the BP to normal level[177] in the following 24–48 h gradually. The details of BP reduction requirements, BP reduction objectives, drug selection and dosage are shown in Table 21.

For elderly patients with hypertension urgencies, it is recommended that on the basis of stable, moderate and long-acting oral antihypertensive drugs, short-or medium-effect oral drugs should be added to avoid intravenous drug therapy. Being monitored, the BP can be slowly reduced to 160/100 mmHg in 24–48 h, and the dosage can be adjusted in the clinic after 2–3 days. After that, the long-acting drugs can be used. BP should achieve the final target level.

3.4.9 Hypertension with atrial fibrillation

The prevalence of atrial fibrillation (AF) increases with age. The incidence of AF is 3%–4%[196] in patients over 65-years old, and 80% of patients with AF have hypertension. AF is a common concomitant disease of hypertension.[197] AF significantly increases the risk of stroke and heart failure in patients with hypertension, and increases the mortality of patients. Tight control of hypertension is the key to the prevention and treatment of hypertension accompanied with AF. Elderly patients with hypertension need further assessment of the risk of thrombosis and bleeding, anticoagulation therapy should be given actively, the treatment should be individualize, whether practice "rhythm" control or "ventricular rate" control is determined by the specific circumstance. Recommendation for the management of elderly patients with hypertension and AF are illustrated in the following Table 22.

3.4.10 Perioperative management of hypertension

Perioperative hypertension refers to SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or the BP increases more than 30%

Table 21. Specification, targets and drug selection for treatment of hypertension emergencies.

Clinical presentations	Specification	Goal	Drug types and dosage	Class	Level
Hypertensive encephalopathy.[178,179]	Brain perfusion should be guaranteed while lowering BP. SBP should be reduced by 20%–25% within one hour after drug administration, but no more than 50%.	160–180/100–110 mmHg	Urapidil (10–50 mg *i.v.*, 6–24 mg/h) Labetalol (20–100 mg iv, 0.5–2 mg/min *i.v.*, no more than 300 mg/24 h) Nicardipine (0.5–10 μg/kg/min *i.v.*)	Ⅰ	C
Cerebral hemorrhage.[180,181]	When SBP is more than 220 mmHg in patients with acute cerebral hemorrhage, active intravenous antihypertensive treatment is needed while the BP should be closely monitored. When SBP is more than 180 mmHg, intravenous antihypertensive treatment should be adjusted and guided by clinical manifestations.	SBP < 180 mmHg	Urapidil (10–50 mg *i.v.*, 6–24 mg/h) Labetalol (20–100 mg *i.v.*, 0.5–2 mg/min *i.v.*, no more than 300 mg in 24 h)	Ⅱa	B
Subarachnoid hemorrhage.[182]	Prevent exacerbation of hemorrhage and excessive decrease of BP, which may cause transient neurological deficits and delayed diffuse lethal cerebral vasospasm.	SBP < 150–160 mmHg	Nicardipine (0.5–10 μg/kg/min *i.v.*) (20–100 mg *i.v.*, 0.5–2 mg/min *i.v.*, no more than 300 mg in 24 h) Esmolol (250–500 μg/kg *i.v.*, there after 50–300 μg/kg/min *i.v.*)	Ⅰ	C
Cerebral infarction.[183–185]	Generally no need for tight control of BP, slightly higher BP is beneficial to perfusion of ischemic area, unless BP ≥ 200/110 mmHg or with heart failure, aortic dissection, hypertensive encephaloathy, *etc*. If urgent thrombolytic therapy is considered, in order to prevent hypertensive cerebral hemorrhage, antihypertensive treatment should be initiated when BP ≥ 185/110 mmHg.	Reduce BP by no more than 25% in 24 h	Urapidil (10–50 mg *i.v.*, 6–24 mg/h) Labetalol (20–100 mg *i.v.*, 0.5–2 mg/min *i.v.*, no more than 300 mg in 24 h) Nicardipine (0.5–10 μg/kg/min *i.v.*)	Ⅱa	B
Malignant hypertension with or without renal damage.[186–188]	Avoid violent fluctuation of BP, steadily reduce BP and ensuring renal perfusion.	< 140/90 mmHg	Diuretics Urapidil (10–50 mg *i.v.*, 6–24 mg/h) Nicardipine (0.5–10 μg/kg/min *i.v.*) Labetalol (20–100 mg *i.v.*, 0.5–2 mg/min *i.v.*, no more than 300 mg in 24 h)	Ⅰ	C
Acute heart failure.[56,158,189–191]	It is often manifested as acute pulmonary edema. In order to relieve symptoms and reduce congestion, vasodilators combined with diuretics are recommended.	< 140/90 mmHg	Sodium nitroprusside (0.25–10 μg/kg/min *i.v.*) Nitroglycerine (5–100 μg/min *i.v.*) Urapidil (10–50 mg *i.v.*, 6–24 mg/h) Diuretics	Ⅰ	C
Acute coronary syndrome.[192–194]	Reduce BP and reduce oxygen consumption of myocardium, but should not affect coronary perfusion pressure and coronary blood flow, prevent reflex tachycardia.	< 140/90 mmHg	Nitroglycerine (5–100 μg/min *i.v.*) Esmolol (250–500 μg/kg *i.v.*, thereafter 50–300 μg/kg/min *i.v.*) Diltiazem (10 mg iv, 5–15 μg/kg/min *i.v.*) Urapidil (10–50 mg *i.v.*, 6–24 mg/h)	Ⅰ	C
Aortic dissection.[195]	Dilate blood vessels, control heart rate, depress myocardium contraction, rapidly reduce and maintain BP at the lowest possible level on the premise of ensuring organ perfusion; beta-blocker and non-dihydropyridine calcium channel blocker are preferred for intravenous treatment, other drugs, such us urapidil, sodium nitroprusside, nicardipine *etc*., may be added when necessary.	SBP < 120 mmHg	Esmolol (250–500 μg/kg *i.v.*, 50–300 μg/kg/min *i.v.*) Labetalol (20–100 mg *i.v.*, 0.5–2 mg/min *i.v.*, no more than 300mg in 24h) Diltiazem (10 mg *i.v.*, 5–15 μg/kg/min *i.v.*) Urapidil (10–50 mg *i.v.*, 6–24 mg/h) Sodium nitroprusside (0.25–10 μg/kg/min *i.v.*) Nicardipine (0.5–10 μg/kg/min *i.v.*)	Ⅰ	C

BP: blood pressure; SBP: systolic blood pressure.

of the baseline BP during the period from the decision of the surgical treatment to almost the end of the surgical-related treatment. About 25% of patients underwent non-cardiac surgery[209] and 80% of patients underwent cardiac surgery[210,211] had perioperative hypertension; and the occurrence of intraoperative hypotension should be aware. Therefore, the purpose of perioperative BP control is to ensure blood perfusion of important organs, maintain cardiac

Table 22. Recommendation for the management of elderly patients with hypertension and AF.

Recommendation	Class	Level
Short-term electrocardiogram and subsequent continuous electrocardiogram monitoring for at least 72 h are recommended for patients with TIA or ischemic stroke.[198–200]	Ⅰ	B
Patient with atrial fibrillation, especially those undergoing anticoagulation therapy should control BP to < 140/90 mmHg.[201–203]	Ⅱa	B
ARB and ACEI are recommended for antihypertensive therapy to prevent new AF and recurrence of paroxysmal AF.[103,201,204,205]	Ⅰ	B
All patients with CHA_2DS_2-VASc ≥ 2 points for males and ≥ 3 points for females) are recommended to take oral anticoagulants for anticoagulation therapy.[206,207]	Ⅰ	A
Radiofrequency ablation is recommended for patients with symptomatic paroxysmal AF whose pharmacological therapy is ineffective.[208]	Ⅰ	A
Radiofrequency ablation should be considered for patients with symptomatic long-term persistent AF whose pharmacological therapy is ineffective.	Ⅱa	C

ACEI: angiotensin-converting-enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin receptor blocker; BP: blood pressure.

Table 23. Recommendation for perioperative management of hypertension in the elderly.

Recommendation	Class	Level
For elective surgery, it is recommended to postpone the operation of patients with SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg.	Ⅱa	C
The perioperative BP control target of elderly patients with hypertension should be less than 150/90 mmHg. If diabetes mellitus or chronic nephropathy exists and the drug is well tolerated, the BP should be further reduced to less than 140/90 mmHg.	Ⅱa	C
In addition to the absolute value requirement of BP, perioperative BP fluctuation should not exceed 10% of the baseline.	Ⅱa	C
For those who take beta blockers chronically, it is not recommended to interrupt the use of beta blockers before operation.[212]	Ⅲ	B
Elderly patients taking ACEI or ARB should be discontinued before non-cardiac surgery.	Ⅱa	C

ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; BP: blood pressure; DBP: diastolic blood pressure; SBP: systolic blood pressure.

function and reduce perioperative complications. Recommendation for perioperative management of hypertension in the elderly are illustrated in the following Table 23.

3.5 Abnormal fluctuation of BP in the elderly

3.5.1 Elderly hypertension with orthostatic BP fluctuation

The elderly hypertension with orthostatic BP fluctuation include the following:

(1) Orthostatic hypotension (OH). OH is defined as a decrease in SBP of at least 20 mmHg and/or a decrease in DBP of at least 10 mmHg when standing up from a lying position (or head tilting of over 60°); it is classified as early (≤ 15 s), classical (within 3 min), and delayed type (> 3 min) according to its occurrence time.[213,214]

OH occurs more easily among elderly hypertensive patients due to an increase in arterial stiffness, a decrease in baroreflex sensitivity, a decline in muscle pump function, dysfunction in regulating effect of autonomic nervous system (ANS), a decrease in ability of effective blood volume of neurohumoral regulation, inappropriate medications, *etc*. There may be no clinical manifestation in patients with OH, and severe ones may be bedridden; its common clinical symptoms include fatigue, dizziness, lightheadedness, faint, and falling down, and the uncommon ones include pain in the neck, shoulder, back, and weakness, *etc*.[215] OH with lying hypertension may occur in part of patients, *i.e.*, SBP ≥ 150 mmHg or DBP ≥ 90 mmHg in the lying position.[216] OH is associated with an increased risk of cardiovascular death, all-cause death, coronary heart disease (CHD) events, heart failure, and stroke,[217,218] and it may also increase the risk of repeating falls and frailty,[219] thereby severely affecting their quality of life (QoL). Therefore, measurement of BP in the lying and standing positions are needed in the process of diagnosis and treatment among elderly patients with hypertension.[220,221]

The main goals for treatment of elderly hypertensive patients with OH include lowering BP in a smooth and slow manner, decrease in occurrence of OH, and prevention of falling down. First, stable BP should be maintained, and antihypertensive drugs that could increase cerebral blood flow should be selected, such as ACEI or ARB, which are initiated from small dose and continued in a slow dose-escalation way every other 1–2 weeks, and excessive BP-lowering should be avoided.[222] Second, patients should move slowly when standing up; bed rest time should be decreased as far as possible, and medications that could exacerbate OH must be avoided, such as α receptor blockers, diuretics, and tricyclic antidepressants (TCAs).[222] Symptoms related to position intolerance could be improved by physical or breathing resistance, including standing while

crossing both legs, squatting position, tension state of muscles in lower limbs, wearing stretch socks and abdominal belts, slow and deep breath, inhaling in with noses, exhaling by pouting.[215,223] If OH or related symptoms of position intolerance still persist, especially the neurogenic OH, after non-drug therapy, drug therapy could be selected. Midodrine is the first-line drug for treatment of OH recommended by USA Food and Drug Administration (FDA), and other medications include droxidopa and fludrocortisone. The specific drug dose, side effects, and precautions for the treatment of OH are presented in Table 24.[213,223] Given multiple adverse reactions of the above medications and individual difference among patients, drug therapy should be carefully used by clinicians.

(2) OH complicated with lying hypertension is a kind of special BP fluctuation. Hypoperfusion caused by OH and target-organ damage due to lying hypertension could result in damage to patients. For those patients, individualized therapeutic regimens should be focused. Generally, the head of a bed should be elevated at night (10°–15°), and supine position at daytime and drinking water within one hour before sleep should be avoided.[224] BP-lowering treatment should be performed according to supine BP level; the use of small-dose and short-acting antihypertensive drugs is recommended before sleep at night, such as captopril or losartan; meanwhile, middle and long-acting antihypertensive drugs or diuretics should be avoided.[216,225,226] Midodrine or fludrocortisone is recommended early in the morning in patients who have significant OH symptoms at daytime.

3.5.2 Abnormal circadian rhythm of BP

According to the decrease rate of nocturnal BP (22:00–8:00) compared to daytime BP (8:00–22:00), the circadian rhythm of BP is classified as: dipper: 10%–20%, non-dipper): < 10%, extreme dipper: > 20%; if nocturnal BP is higher than daytime BP, it is called inverted dipper. According to statistics, the incidence of non-dipper BP can be as high as 69% among the elderly over 60-year old, more than three times than that of young and middle-aged people. About 83.3% of the elderly who are over 80-year old lost normal dipper BP rhythm.[227] Abnormal circadian rhythm of BP is an independent predictor of target-organ damage,[228] cardiovascular events,[229] stroke,[230] and death.[231]

(1) Lowering nocturnal BP in patients with non-dipper or inverted dipper type and restoring dipper-type rhythm can significantly reduce cardiovascular risk and adverse events.[232] First, BP rhythm can be explored by HBPM or 24 h ambulatory BP. Appropriate aerobic exercise (about 30 min) can be performed at night (17:00–18:00) to help correct abnormal BP rhythms.[233] The first choice for drug therapy is the long-acting antihypertensive drug that can lower BP in a stable manner in 24 h: single drug or drug combination. If nocturnal BP control remains unsatisfactory, one or several long-acting antihypertensive drugs can be administrated at night or before sleep, which can help over 70% of patients restore dipper BP rhythm.[234] If the nocturnal BP is still high after using the above method, according to the action time of the drug, based on the long-acting antihypertensive drug, the middle and short-acting antihypertensive drugs can be added before sleep. However, the possibility of too low nocturnal BP and occurrence of OH when getting up at night should be considered.

(2) Patients with extreme dipper BP need to lower their daytime BP. Long-acting antihypertensive drugs (such as amlodipine, felodipine sustained-release tablets, and nifedipine controlled-release tablets, etc.) should be administrated in the morning on the basis of non-drug therapy (such as physical exercise), which can lower daytime BP while nocturnal BP will not be decreased excessively. If daytime BP control is still not ideal, by combining with the characteristics of BP fluctuation and pharmacodynamics, the combination of long-acting plus middle and short-acting drugs can be selected to further control daytime BP; however careful attention to the increased risk of OH due to middle and short-acting antihypertensive drugs must be considered. The administration of antihypertensive drugs at night should be avoided otherwise the extreme dipper BP model will be aggravated.

Table 24. Recommended drugs for the treatment of OH.

Drugs	Drug category	Dose	Side effects	Precautions
Midodrine	α receptor agonist	Recommended dose: 2.5–10 mg, TID.	Purpura, urinary retention, and lying hypertension.	Its use 4–5 h before sleep should be avoided.
Droxidopa	Precursor substance of norepinephrine	Initial dose: 100 mg, TID, and dose escalation of 100 mg every other 3–7 d until appropriate maintenance dose.	Lying hypertension, headache, dizziness, and nausea.	It should be carefully used in patients with congestive heart failure and chronic renal insufficiency.
Fludrocortisone	Effects of adrenal mineralocorticoid receptors	Generally, the initial dose is 0.1 mg with being less than 0.3 mg every day.	Lying hypertension, edema, hypokalemia, headache, and adrenal function inhibition may occur in severe cases.	It should be forbidden in patients with heart failure, kidney failure, or severe hypertension.

3.5.3 Postprandial hypotension (PPH)

PPH is a condition in which there is a SBP drop of over 20 mmHg within 2 h after eating a meal; or SBP ≥ 100 mmHg before a meal, and < 90 mmHg after a meal; or the decrease in postprandial BP does not reach the above criteria, but symptoms of postprandial myocardial and cerebral ischemia occur. Its incidence rate among elderly patients hospitalized in China is 80.1%.[235] The treatment of PPH includes:

(1) Non-drug therapy. (a) drinking water therapy: patients with autonomic nervous system dysfunction drinking 350–480 mL of water before a meal can lower the postprandial BP by 20 mmHg, and related symptoms can be effectively reduced.[236] The optimal water intake should be individualized based on patients' specific conditions. This therapy should be carefully used in patients with severe HF and end-stage renal disease who need water restriction; (b) eat small meals more often: it can reduce the amount and duration of blood transferring to the internal organs, which may be beneficial to patients with PPH, but the association between meal intake and BP remains to be further studied; (c) reducing carbohydrate intake: compared to protein and fat, carbohydrates are the fastest in the gastric emptying and have the strongest inductive effect of insulin release; therefore, eating food rich in carbohydrates is more likely to cause a rapid decline in postprandial BP.[237] Chinese breakfast is mainly based on carbohydrates, so hypotension after breakfast is the most common. Dietary ingredients can be changed properly, and appropriate reduction in carbohydrate intake is recommended; and (d) postprandial exercise: the elderly with intermittent low-intensity exercise for 20–30 min after a meal (such as 30 meters of walking, once every 30 min) can help improve cardiac output, reduce the decrease degree of SBP and the incidence of falls;[238] however, excessive exercise may have the opposite effect. Appropriate exercise mode, intensity and time need further exploration.[239]

(2) Drug therapy. Excessive BP level before a meal can lead to more serious PPH. Therefore, appropriate BP-lowering treatment should be performed to make BP reach the standard, especially morning BP level should be effectively reduced.

The elderly administrated with 50 mg of α-glucosidase inhibitor acarbose can significantly lower blood flow in the gastrointestinal tract after meals, reduce the decrease degree of postprandial SBP and DBP, thus effectively controlling related symptoms,[240] which is suitable for elderly patients with diabetes. Other possibly effective medications include caffeine, octreotide, guar gum, dipeptidyl peptidase-4 inhibitor, denopamine plus midodrine and vasopressin, etc., however, given unclear use methods, lack of effective validation, and many side effects, it is hard for clinical application.

3.5.4 Morning BP surge

It is defined as the average SBP within two hours after getting up in the morning-the lowest value of SBP during nighttime sleep (the average SBP of the lowest values of nocturnal BP for three times) ≥ 35 mmHg.[23] The incidence of morning BP surge (MBPS) in the elderly in China is 21.6%, and patients with hypertension are more common than normal persons.[241,242] The treatment of MBPS includes: (1) lifestyle interventions: it includes smoking cessation, alcohol restriction, low-salt diet, avoiding emotional fluctuation, maintaining good nighttime sleep, staying in the bed for a while and moving slowly after getting up in the morning, avoiding intense activities immediately after getting up; (2) drug therapy: the use of long-acting antihypertensive drugs that can lower BP level in a stable manner in 24 h can control the large fluctuations of BP in the morning, and reduce MBPS caused by not taking medications on time or missing. In addition, maintaining a modest decline in nocturnal BP (dipper BP) can effectively control MBPS.[243] Hypertensive patients with non-dipper or inverted dipper type can choose to take long-acting antihypertensive drugs before sleep. Domestic studies have shown that taking nifedipine controlled-release tablets at 19:00–21:00 in the evening can significantly reduce the elevation rate of BP in the morning compared with that at 6:00–8:00 in the morning.[244] For those with extreme dipper, based on long-acting antihypertensive drugs, the use of short-acting ones to inhibit MBPS is recommended.

3.5.5 Long-term BP variability

Seasonal changes in BP increase with age, especially for elderly hypertensive patients whose BP is significantly higher in winter than in summer,[245] which is associated with temperature drop, neuroendocrine activation, and increase in the load of renal sodium excretion.[246] Therefore, for elderly hypertensive patients, the medication regimens should be adjusted in time according to seasonal changes.

3.5.6 White coat hypertension

Its incidence in the whole population is approximately 13%, and it occurs frequently (up to 40%) among the elderly.[21] HBPM and ABPM can be used to identify white coat hypertension. It is not completely benign, with a higher

risk of developing sustained hypertension[247] and type 2 diabetes,[248] and an increased overall risk of cardiovascular events.[249] Therefore, screening on cardiovascular risk factors should be improved for those patients, and lifestyle interventions and regular follow-up visit are recommended.

3.6 Elderly secondary hypertension

Secondary hypertension is common among elderly hypertensive patients. It is commonly caused by renal parenchymal disease, renal artery stenosis, primary aldosteronism (PA), pheochromocytoma/paraganglioma.[250] Moreover, combination drug therapy is often performed in the elderly complicated with other diseases, and attention to the hypertension related to drugs (such as non-steroidal anti-inflammatory drugs, licorice, *etc*.) should be considered.

3.6.1 Renal parenchymal hypertension

Renal parenchymal hypertension (RPH) is defined as the elevation of BP resulting from renal parenchymal disease (such as glomerulonephritis, interstitial nephritis, *etc.*).

Reminders of RPH[251] include (1) Markers of renal injury: albuminuria [urinary albumin excretion rate ≥ 30 mg/24 h; the ratio of urinary albumin and creatinine ≥ 30 mg/g (or ≥ 3 mg/mmol)], abnormal urine sediment, renal tubular-related lesions, histological abnormalities, structural abnormalities in imaging findings, and history of renal transplantation; (2) Decrease in glomerular filtration rate: estimated glomerular filtration rate < 60 mL/ (min·1.73 m^2).

Renal ultrasonography is the most common and preferred method of examination. CT and MRI are often used as important auxiliary examinations. Renal biopsy is the gold standard for the diagnosis of kidney diseases.

As preferred antihypertensive drugs, ACEI and ARB are especially suitable for those patients with proteinuria; dihydropyridine CCB is effective in patients with obvious renal dysfunction, and its antihypertensive effect is not affected by high-salt diet; diuretic is suitable for those with volume overload, and its combination with ACEI or ARB can reduce the risk of hyperkalemia; β blockers are effective for those patients with tachyarrhythmia, increase in sympathetic activity, CHD or cardiac dysfunction.

3.6.2 Primary aldosteronism

Primary aldosteronism (PA) is defined as the adrenal hyperplasia or tumor, and excessive secretion of aldosterone results in sodium retention and potassium excretion in the body, thus increasing blood volume and inhibiting activity of renin-angiotensin system. Its main clinical manifestation is hypertension with or without hypokalemia.

Conditions needing for PA screening are as follows:[252,253] (1) persistent BP > 160/100 mmHg, resistant hypertension; (2) hypertension complicated with spontaneous or diuretic-related hypokalemia; (3) hypertension with adrenal incidentaloma; (4) family history of early-onset hypertension or hypertensive patients with a family history of early-onset cerebrovascular accidents (< 40 years old); (5) first-degree relatives with hypertension in patients with PA; and (6) hypertension with obstructive sleep apnea.

The normal saline test and captopril test can be used for PA confirmation, and the screening index is the ratio of plasma aldosterone to renin activity. For all patients with confirmed PA, adrenal CT is recommended to identify adrenal lesions. If the patient is willing to undergo surgery and surgery is feasible, venous sampling of bilateral adrenal glands is recommended to determine whether there is a dominant secretion.

Laparoscopic unilateral adrenalectomy is recommended for patients with confirmed aldosteronoma or unilateral adrenal hyperplasia. If the patient has contraindications or is unwilling to undergo surgery, aldosterone receptor antagonist therapy is recommended; however, the effect of adrenalectomy is poor in patients with idiopathic hyperaldosteronism (IHA) and glucocorticoid-remediable aldosteronism (GRA), therefore, low-dose glucocorticoids should be preferred.[252]

3.6.3 Renal artery stenosis

For elderly patients, the atherosclerosis leads to stenosis of unilateral or bilateral renal artery trunk or branch, thus resulting in an elevation in BP caused by renal ischemia, which is called renovascular hypertension (RVH).

Conditions needing for renal artery stenosis screening are as follows:[254] (1) sustained hypertension of grade 2 or above with clear CHD, arterial stenosis of four limbs or carotid stenosis; (2) hypertension with continuous mild hypokalemia; (3) hypertension with periumbilical vascular murmur; (4) previous hypertension can be controlled, however, BP is suddenly difficult to control without the change of antihypertensive drugs; (5) resistant or malignant hypertension; (6) severe hypertensive patients with normal left ventricular ejection fraction (LVEF), but transient pulmonary edema recurs; (7) renal dysfunction or asymmetrical renal atrophy unable to be explained with other causes; (8) significant increase in blood creatinine or with markedly decrease in BP after taking ACEI or ARB; and (9) DBP level is maintained above 90 mmHg.

Ultrasound examination of bilateral renal functions is a first-line method of examination in clinical practice, which

can reveal changes in renal parenchyma, renal pelvis, renal artery trunk and intrarenal blood flow. CTA has a higher spatial resolution and can provide detailed information regarding the extent and forms (plaques, calcification, dissection, *etc.*) of renal artery trunk and branch lesions, and conditions of the accessory renal artery. Renal angiography is the "golden standard" for diagnosis of renal artery stenosis. It can show the location and extent of lesions in a clear and accurate way, and the concurrent interventional therapy can be performed.

ACEI/ARB is the first-line drug for treatment of RVH, but it should be noted that ACEI/ARB should be used with caution in patients with solitary kidney or bilateral renal artery stenosis. Patients undergoing renal artery stenting need to meet two key points:[254] (1) renal artery stenosis ≥ 70%, and a causal relationship between stenosis and elevated BP can be demonstrated; and (2) resistant hypertension or hypertension of grade 3 without the use of antihypertensive drugs. Open surgery is needed for patients with severe renal artery stenosis who are not suitable for vascular interventional therapy based on anatomical characteristics of renal artery, failure of interventional therapy or serious complications, and renal artery stenosis with abdominal aortic disease.[255]

3.6.4 Obstructive sleep apnea-hypopnea syndrome

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterized by repeated, frequent apnea and hypopnea during sleep. Most of patients belong to OSAHS clinically.

Conditions needing for OSAHS screening are as follows:[256] (1) obesity; (2) abnormal anatomical structure of the nasopharynx and maxillofacial region; (3) snoring during sleep, obvious daytime sleepiness, morning headache, and dry mouth; (4) resistant hypertension or masked hypertension, morning hypertension, or hypertension with rhythm showing "dipper" or "inverted dipper" changes; (5) recurrent angina pectoris that is difficult to control at night; (6) arrhythmia that is difficult to correct at night; (7) refractory congestive heart failure; (8) intractable refractory diabetes and insulin resistance; (9) pulmonary hypertension of unknown cause; and (10) nighttime wakefulness or nocturnal paroxysmal diseases.

Polysomnography (PSG) is the golden standard for the diagnosis of OSAHS;[256,257] according to apnea hypoventilation index (AHI), *i.e.*, the average number of sleep apnea and hypopnea per hour, adult OSAHS can be classified as mild, moderate, and severe type; and $5 < AHI \leq 15$ indicates mild type, $15 < AHI \leq 30$ moderate type, and $AHI > 30$ severe type.

At present, non-invasive positive pressure ventilation (NIPPV) is the most effective treatment for adult OSAHS and the continuous positive airway pressure (CPAP) is the most commonly used method.[258]

3.6.5 Drug-related hypertension

Drug-related hypertension is defined as an elevation of BP caused by the pharmacological and/or toxicological effects of drugs, interaction among drugs, or the improper administration of drugs. Common drugs that result in hypertension include: non-steroidal anti-inflammatory drugs, hormones (estrogen, erythropoietin, glucocorticoids), antidepressants (monoamine oxidase inhibitors, tricyclic antidepressants, *etc.*), immunosuppressants (cyclosporine A), angiogenesis inhibitors and licorice, etc., and the main mechanisms of BP elevation include sodium retention, increase in sympathetic excitability and vasoconstriction, *etc.*[259,260]

Conditions needing for drug-related hypertension screening are as follows:[259] (1) the increase in BP is reasonably related to the time of medication; (2) the pharmacological action of the drug may cause hypertension; (3) there are previously reported studies that single or combination use of the drug could lead to hypertension; (4) BP can be restored to the pre-administration level after drug withdrawal; and (5) drug challenge test can lead to elevation of BP again.

Treatment principles include:[259] (1) immediate discontinuation of drugs that cause hypertension; (2) for patients who cannot stop the use of drugs that cause hypertension due to conditions or whose BP cannot be restored, BP monitoring and antihypertensive treatment are recommended; (3) appropriate BP-lowering regimens should be selected according to specific drugs causing BP elevation and mechanisms affecting antihypertensive effect; and (4) active treatment for complications should be performed.

4 Community support and remote management

4.1 Community support

Given the characteristics of elderly hypertensive patients, it is extremely important for the support from the community environment. Elderly patients have great fluctuations in BP, and OH, PPH, abnormal circadian rhythm of BP, WCH, *etc.*, easily occur among them; meanwhile, these patients are often accompanied by multiple diseases; furthermore, multiple drugs are often taken concurrently, therefore, medication guidance should be individualized; their self-care ability is relatively decreased, and they often have difficulty in

moving; fortunately community health care is convenient and fast integrating treatment and prevention; community medical personnel have a better understanding of residents' health status and living habits, so intervention measures are more targeted. Guided by relatively familiar and trusted community workers, it can improve their compliance. In addition to medical services, the community can provide better family and humanistic care.

4.1.1 Follow-up support

Elderly hypertensive patients require systematic, long-term follow-up and management, which can be accomplished depending on the community. Community follow-up can take many ways, such as household follow-up, home monitoring, and remote services.

4.1.2 Health education

Most of hypertensive patients seek medical service in the primary health care institutions, and primary medical care or health management organizations and elementary health care workers in community health service centers (stations), township health centers, village health centers, healthcare centers, health education institutions, *etc.*, play the main role in the hypertension education.

4.1.3 Environmental support

The favorable community environment should be created to promote the acceptance of healthy lifestyles for elderly hypertensive patients, and the elderly with better activity should be encouraged to return to the community health service centers for regular follow-up and health education, and it will be convenient for patients to seek medical treatment when myocardial infarction (MI), stroke, and other related symptoms occur.

4.1.4 Humanistic care

Due to rapid changes in social roles, the elderly are prone to have adverse psychological changes, and there will be problems such as functional decline, limited activity, and emotional loneliness. In the absence of appropriate care, hypertension management cannot achieve ideal effects. Psychological counseling can be conducted based on the characteristics of the elderly. For empty nesters, regular visit should be performed by neighborhood committees and medical institutions to provide emotional support and home medical services.

4.2 Remote management

4.2.1 Advantages of remote management of hypertension

Remote dynamic monitoring can help the primary care doctors to grasp the patient's BP fluctuations in real time, predict the disease change, and take timely treatment measures to prevent the exacerbation of the disease, thus realizing the individualized treatment for patients. In the meantime, excellent expert resources can also be used through remote video and other technologies for training, counseling, and guidance in patients to improve the medical treatment.

4.2.2 Contents of remote management of hypertension

It mainly includes timely data monitoring and risk assessment, optimal treatment, lifestyle interventions, enrichment of health education contents, and treatment of emotional problems in the elderly patients.

On the basis of the above functions, remote management of hypertension takes the data monitoring as the pointcut, and an accurate management system for prevention, monitoring, intervention and protection can be created for the elderly hypertensive patients. By integrating the timeliness, accessibility, and individuality of internet technology with the particularity of the elderly hypertensive group, the optimal management can be achieved.

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