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2023 Guideline for the management of hypertension in the elderly population in China

Hypertension Branch of Chinese Geriatrics Society, Beijing Hypertension Association, National Clinical Research Center of the Geriatric Diseases , Qi HUA[1,✉], Li FAN[2,✉], Zeng-Wu WANG[3,✉], Jing LI[1,✉]

1. Xuanwu Hospital, Capital Medical University, Beijing, China; 2. Chinese PLA General Hospital, Beijing, China; 3. Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
✉ Correspondence to: huaqi5371@sina.com (HUA Q); fl6698@163.com (FAN L); wangzengwu@foxmail.com (WANG ZW); shpxbb@sina.com (LI J)
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Preamble

Hypertension is one of the most common chronic diseases and the primary risk factor for stroke, myocardial infarction and even cardiovascular death. More than half of the elderly population has high blood pressure. Elderly people are a unique group, and strategies for the prevention, diagnosis, evaluation, and treatment of hypertension in elderly individuals differ significantly from those in the general population. To improve the prevention and treatment of hypertension in the elderly population in China, the Hypertension Branch of Chinese Geriatrics Society, the Beijing Hypertension Association, and the National Clinical Research Center of the Geriatric Diseases (Chinese PLA General Hospital, Beijing, China and Xuanwu Hospital, Capital Medical University, Beijing, China) jointly established an expert committee based on the "2019 Chinese guideline for the management of hypertension in the elderly". The Revision Committee of the "2023 Guideline for the management of hypertension in the elderly population in China" organized domestic experts in the field of hypertension and completed the literature search, framework setting, content writing, evidence level and recommendation level evaluation with reference to the procedures formulated by international and domestic guidelines. This led to a new, evidence-based consensus after many organized discussions and revisions. The blood pressure measurement in elderly individuals, blood pressure targets, characteristics of elderly hypertension, functional preservation, multiple medications, treatment of specific populations and blood pressure management strategies were discussed in detail.

Compared with the 2019 version of the guideline, the 2023 version of the guideline cites newly published epidemiological and clinical research evidence based on the elderly hypertensive population in China. Recognition of the importance of blood pressure measurement in the diagnosis and treatment of hypertension in elderly people has enriched the management of elderly hypertensive cases complicated by frailty, cognitive impairment and multiple organ dysfunction; has led to updates in the drug treatment recommendations for geriatric hypertension and its accompanying diseases; and has enabled expansion of the treatments for high blood pressure in elderly individuals. The scope of this special population of blood pressure patients necessitates further optimization of the management strategy of hypertension in elderly individuals. The 2023 version of the guideline closely integrates the characteristics and clinical aspects of hypertension in the elderly in China and combines evidence with practice. It is believed that the publication of the "2023 Guideline for the management of hypertension in the elderly population in China" will play an important role in promoting the prevention and treatment of hypertension in the elderly in China.

OVERVIEW

Class of Recommendations and Level of Evidences

The definitions and specific expressions of the recom-

mendation categories and evidence grading in this guideline are shown in Tables 1 & 2.

Definition and Classification of Hypertension in the Elderly

Age ≥ 65 years, blood pressure (BP) was measured 3 times on different days without antihypertensive drugs, systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg (1 mmHg = 0.133 kPa), that is, a diagnosis of geriatric hypertension. For older adults who have been diagnosed with hypertension and are receiving antihypertensive medication, although BP < 140/90 mmHg, hypertension in elderly individuals should also be diagnosed. The definition and classification of hypertension in the elderly population are the same as those in the general adult population (Table 3).

When the systolic blood pressure and the diastolic blood pressure are graded at different levels, the higher-level category will prevail. Isolated systolic hypertension is graded according to the systolic blood pressure level.

The above definitions and classifications are based on the clinic seated BP measurement results. In recent years, the application of home self-measurement BP and ambulatory BP monitoring has become increasingly widespread in China. On the premise of using BP measurement tools that meet the measurement standards and standard measurement operations, the results of home self-measured BP and ambulatory BP monitoring can also be used as the basis for the diagnosis and efficacy evaluation of hypertension. The diagnostic criteria for office BP, home self-measurement BP, and ambulatory BP measurement are shown in Table 4.

Epidemiological Trend and Current Status of Prevention and Treatment of Hypertension in the Elderly

The 1991 National Hypertension Sampling Survey showed that the prevalence of hypertension in elderly people aged ≥ 60 years in China was 40.4%,[2] the 2002 National Nutrition Survey showed that the prevalence of hypertension was 49.1%,[3] the 2012–2015 national hypertension stratified multistage random sampling cross-sec-

Table 1 Recommended categories.

Recommended category	Definition	Suggested expressions
Class I	Evidence and/or general consensus that the treatment or method is beneficial, useful or effective	Recommended/Indicated
Class II	Inconsistent evidence and/or disagreement about the use/efficacy of the treatment or method	
Class IIa	Evidence/opinion tends to be useful/valid	Should be considered
Class IIb	Insufficient evidence/opinion to establish useful/valid	Can be considered
Class III	Evidence and/or expert consensus that the treatment or method is not useful/ineffective and may be harmful in some cases	Not recommended

Table 2 Level of evidence.

Evidence grading	Definition
Level A	Data from multiple randomized controlled clinical trials or a meta-analysis consisting of randomized controlled clinical trials
Level B	Data from a single randomized clinical trial or multiple large nonrandomized controlled studies
Level C	Data from expert consensus and/or small studies, retrospective studies or registries

Table 3 Definition and classification of blood pressure levels in the elderly population.[1]

Definition and classification	Systolic blood pressure, mmHg	Diastolic blood pressure, mmHg
Normal blood pressure	< 120	< 80
Normal high value	120–139	80–89
Hypertension	≥ 140	≥ 90
Grade 1	140–159	90–99
Grade 2	160–179	100–109
Grade 3	≥ 180	≥ 110
Isolated systolic hypertension	≥ 140	< 90

Table 4 Hypertension diagnostic criteria for office blood pressure and out-of-office blood pressure measurement.[1]

Blood pressure measurement	Diagnostic criteria
Office blood pressure	≥ 140/90 mmHg
Home self-measured blood pressure	≥ 135/85 mmHg
24-hour ambulatory blood pressure, mean	≥ 130/80 mmHg
Daytime, mean	≥ 135/85 mmHg
Nighttime, mean	≥ 120/70 mmHg

tional survey data showed that the prevalence of hypertension was 53.2%,[4] and the prevalence of hypertension showed an overall increasing trend. According to the survey data in 2018, the prevalence of hypertension among people aged ≥ 60 years, ≥ 70 years, and ≥ 80 years was 54.4%, 65.2%, and 66.7%, respectively.[5] From 2004 to 2018, the prevalence of hypertension in people aged 60–69 years showed a slow upward trend over time, regardless of sex.[6]

The survey data from 2012 to 2015 showed that the awareness rate, treatment rate and control rate of hypertension among people aged 60 years and above were 57.1%, 51.4% and 18.2%, respectively, which were significantly higher than those in 2002 (Table 5).[3] The survey data in 2018 showed that the hypertension awareness rate and treatment rate among people aged ≥ 60 years, ≥ 70 years, and ≥ 80 years were nearly 50%, but the control rate was 13.4% to 14.8%, slightly higher than that in young people.[5] From 2004 to 2018, regardless of sex, the three rates of hypertension (awareness rate, treatment rate and control rate) in people aged 60–69 years increased significantly.[6] Notably, the BP control rate in elderly hypertensive patients did not improve with an increasing number of medications taken.[7]

Characteristics of Hypertension in the Elderly

With age, the elasticity of large arteries decreases and arterial stiffness increases; baroreceptor reflex sensitivity and beta-adrenergic system reactivity decrease; and the ability of the kidney to maintain ion balance decreases, manifested as increased volume load and increased peripheral vascular resistance.[8] Therefore, elderly hypertension has the following characteristics:

(1) The SBP is mainly increased: increased SBP and increased pulse pressure are common in elderly hypertensive patients. According to Chinese population statistics, the prevalence rate of isolated systolic hypertension in the elderly population is 29.0% to 31.9%, and the number of patients accounts for 56.9% of the total number of elderly patients with hypertension, while the prevalence of isolated diastolic hypertension in the elderly population is only 1.3%.[4,9] Compared with increased DBP, increased SBP is more closely related to target organ damage, such as the heart, brain, and kidney, and is a more important independent predictor of cardiovascular events. Therefore, antihypertensive treatment in elderly patients should emphasize SBP targets.

(2) BP fluctuates greatly: due to the decreased ability to regulate BP, the BP level of the elderly population is susceptible to fluctuations due to various factors, such as body position, meal, mood, season or temperature, which is called abnormal BP fluctuation. The most common signs are abnormal BP circadian rhythms, orthostatic BP fluctuations, and postprandial hypotension.

The incidence of abnormal BP circadian rhythms in the elderly can be as high as 76.5%, often manifesting as nondippers and reverse dippers.[10] The nighttime BP is less than 10% lower than daytime BP or even higher than daytime BP, which is more common in elderly people.[11] At the same time, orthostatic BP fluctuations can manifest as orthostatic hypotension, orthostatic hypertension, and supine hypertension combined with orthostatic hypotension. The incidence of orthostatic hypotension in the elderly hypertensive population in China is 20.6% to 28.8%,[12,13] and the incidence of orthostatic hypertension is 7.2% to 10.8%.[14,15] Patients with orthostatic hypertension have a higher cardiovascular risk than those with hypertension and orthostatic hypotension. In addition, postprandial hypotension is also a common type of abnormal BP fluctuation in elderly individuals, and the prevalence of postprandial hypotension in nursing home residents ranges

Table 5 Three survey results of the hypertension prevalence, awareness rate, treatment rate and control rate in China.

Year	Age, yrs	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%
2018	60–70	54.4%	51.6%	45.0%	14.6%
	70–80	65.2%	55.7%	50.0%	14.8%
	≥ 80	66.7%	53.9%	48.2%	13.4%

from 24.0% to 30.0%.[16] There is 59.3% in the community elderly population in China,[17] and even as high as 74.7% in the hospitalized elderly patients,[18] and increases with age,[19] which is an important risk factor for syncope, falls, and cardiovascular events.[20,21]

(3) Polypharmacy: elderly hypertensive patients (≥ 80 years old) often have a variety of risk factors and related diseases. The detection rates of diabetes mellitus (DM), hyperlipidemia, coronary heart disease (CHD), renal insufficiency and cerebrovascular disease were 39.8%, 51.6%, 52.7%, 19.9% and 48.4%, respectively.[22] Due to the combination of multiple chronic diseases, polypharmacy is a common phenomenon in the elderly[23]. Research in China shows that the incidence of multiple drug adverse reactions in elderly individuals in the community is 5.8% to 14.2%.[24,25] The incidence of multidrug adverse reactions in elderly hypertensive hospitalized patients was higher, at 30.7%.[26]

(4) Pseudohypertension: in elderly hypertensive patients with severe arteriosclerosis, it may be difficult to compress the brachial artery when the cuff is pressurized, and the measured BP value is higher than the intra-arterial pressure value, which is called pseudohypertension. Relatively accurate BP values can be obtained by noninvasive central arterial pressure detection. The incidence of pseudohypertension increases with age.[27] When the measured SBP is abnormally elevated without associated target organ damage or hypotensive symptoms appear after antihypertensive medication, the possibility of pseudohypertension should be excluded. Pseudohypertension can lead to excessive antihypertensive treatment, and low SBP may lead to an increase in adverse events such as falls and syncope in elderly patients.[22]

With increasing age, the incidence of calcific valvular disease increases, and echocardiography can confirm the diagnosis. In cases of severe aortic valve stenosis, excessive BP should be avoided so as not to affect the blood supply of important organs. If the pulse pressure is too high, the SBP will increase significantly and the DBP level will be lower than 50 mmHg; attention should also be paid to the possibility of aortic insufficiency.

In addition, if symptoms of hypotension occur repeatedly during antihypertensive treatment, white coat hypertension should also be considered. Patients with white coat hypertension account for approximately 15.0% of the total population and 30.0% to 40.0% of hypertension patients,[28] and elderly patients have a particularly high incidence of hypertension, up to 40.0%.[19] Although the morbidity and mortality of cardiovascular disease (CVD) in the white-coat hypertensive population are lower than those in the hypertensive population, they are still higher than those in the normotensive population.[29] Therefore, in the management of hypertension, at the same time, attention should be given to the home self-measured BP and ambulatory BP.

DIAGNOSIS AND EVALUATION

Medical History

For newly diagnosed elderly hypertensive patients, a comprehensive assessment of symptoms and medical history include: (1) course of disease: duration of hypertension, highest BP, antihypertensive treatment status and compliance; (2) past history: whether there is CHD, heart failure (HF), atrial fibrillation (AF), cerebrovascular disease, kidney disease, peripheral vascular disease, DM, dyslipidemia, hyperuricemia, sleep apnea syndrome, abnormal thyroid function, tumor and other diseases and treatment; (3) family history: with or without hypertension, CHD, stroke, kidney disease, DM, and dyslipidemia; (4) whether there are clinical manifestations suggesting secondary hypertension and target organ damage; (5) current medications (especially those that affect blood pressure) and any adverse drug reactions; (6) lifestyle: diet (such as intake of fat, salt, alcohol, coffee, etc.), smoking time and number of cigarettes, physical activity, sleep habits and changes in body mass index; and (7) psychosocial factors: family situation (widowed, living alone, etc.), living environment, educational level, whether there is a history of mental trauma and current mental and psychological state, etc.

Physical Examination

(1) Measure the body mass index, waist circumference and hip circumference; (2) observe for special facial features, central obesity, purpura, hirsutism, exophthalmos, neck blood vessel pulsation and lower extremity edema; (3) palpate the thyroid gland and kidneys for renal enlargement (polycystic kidney) or mass; (4) auscultate the carotid artery, thoracic aorta, abdominal artery and femoral artery for murmurs; (5) thorough cardiopulmonary examinationg; (6) check blood pressure in four limbs (at least both arms), arterial pulses, and neurological signs; and (7) use an ophthalmoscope to check whether the retina is abnormal.

Auxiliary Inspection

Auxiliary inspection is designed to provide an overall as-

sessment of target organ damage and cardiovascular risk and to identify secondary hypertension. In addition to basic examinations such as routine blood and urine tests, blood biochemistry and electrolytes, and electrocardiograms, postprandial monitoring, it is recommended for elderly hypertensive patients to monitor postprandial blood glucose, glycosylated hemoglobin, homocysteine, high-sensitivity C-reactive protein, 24-hour ambulatory BP monitoring and echocardiography, and further carotid artery ultrasound, chest X-ray, fundus examination, pulse wave velocity (PWV), ankle-brachial BP index, head computed tomography or magnetic resonance imaging evaluations and other tests. For suspected secondary hypertension, further investigation should be performed.

BP Measurement

BP measurement is the fundamental means and method for evaluating BP level, diagnosing hypertension and observing the efficacy of antihypertensive drugs. According to the BP characteristics of elderly individuals, elderly hypertensive patients should be encouraged and guided to take home BP measurement and ambulatory BP monitoring and to measure the BP of both upper extremities and limbs and different positions (upright and supine) regularly (e.g., annually).

In-office BP measurement

In-office BP measurement generally refers to the measurement of BP by medical staff in a hospital environment in accordance with BP measurement specifications.[9] BP measurement is a common method for evaluating BP levels and observing the efficacy of antihypertensive agents.

In addition to routine office BP measurement in elderly individuals, the following BP measurements should be performed when necessary:

(1) BP measurement of both upper extremities: for elderly hypertensive patients newly diagnosed or patients suspected with one supraclavicular artery or upper extremity arterial stenosis, BP measurement of both upper extremities should be performed, and the BP of the upper extremity with the higher BP should be selected for diagnosis and long-term management.

(2) BP measurement of extremities: for elderly patients at risk of peripheral arterial disease, especially lower extremity arterial obstructive lesions, it is recommended to use automatic measurement equipment to measure the BP of the extremities synchronously.[30]

(3) Supine and upright BP measurement: for elderly patients who are newly diagnosed, especially elderly patients with Parkinson's disease and other patients with reduced baroreflex function, and patients who may be receiving excessive antihypertensive treatment, it is recommended to perform BP measurements in both the lying and the standing positions.[31] Usually, from the supine position, with standing for 1 min and 3 min, a SBP drop of ≥ 20 mmHg or a drop in DBP ≥ 10 mmHg is defined as orthostatic hypotension.

Out-of-office BP measurement

Out-of-office BP monitoring can more truly reflect the BP status in their living conditions and can identify white coat hypertension and masked hypertension.[32,33] Out-of-office BP monitoring includes home BP monitoring and ambulatory BP monitoring.

(1) Home BP monitoring: also known as BP self-monitoring. It can be used to assess BP control and long-term BP variability over days, weeks, months, or even years. The method is simple and easy to implement and helps to improve the compliance of BP monitoring and treatment in elderly patients and to identify white coat and masked hypertension. Measurement methods[32,34] were as follows: (a) an upper-arm household automatic electronic sphygmomanometer that has passed the international standard program certification is preferred. However, in special cases, such as in cold areas where it is inconvenient to expose the upper arm or for obese people without suitable cuffs, a verified wrist-type sphygmomanometer can be used. The use of finger sphygmomanometers and mercury column sphygmomanometers is not recommended for home BP monitoring. Electronic sphygmomanometers should be calibrated regularly during use, at least once a year; (b) monitoring frequency: it is recommended to measure the BP every morning and evening in the initial treatment stage, in individuals with unstable BP or when adjusting the drug treatment plan (measure 2 to 3 times each time, take the average value, and then measure continually for 7 days, calculating the weekly average). People with stable BP can measure their BP 1 day weekly; in patients on long-term drug treatment, it is recommended to monitor the BP status before taking the drug; (c) keep a daily detailed record of the date, time and all BP readings of each BP measurement so that doctors can guide and evaluate BP monitoring and control effects; and (d) home BP monitoring is not recommended for patients with se-

vere anxiety, combined cognitive impairment, and sleep disorders.

(2) Ambulatory BP monitoring[33]: use an automatic BP measuring instrument to continuously measure the BP level and BP fluctuation state during the individual's daily work and living conditions, especially monitoring the BP during nighttime sleep. Ambulatory BP monitoring can better observe the efficacy of antihypertensive drugs and identify white coat and masked hypertension. Measurement methods[33] were as follows: (a) use ambulatory BP monitors certified by international standard programs and calibrate them regularly; (b) usually, performing measurements every 20–30 min during the day and every 30 min during sleep at night. Valid BP monitoring should be ensured that during the entire 24-hour period, the effective BP readings cover more than 70% of the total monitoring times; (c) according to the ratio of nighttime BP drop compared with the daytime BP level (> 20%, 10%–20%, 0–10%, and < 0), the circadian rhythm of BP can be defined as dipper, nondipper, reverse dipper, or hyperdipper. Other measures derived from ambulatory BP include 24-hour BP variation, smoothing index, morning BP surge, BP load, dynamic arteriosclerosis index, etc; and (d) nocturnal BP monitoring is affected by various factors, such as sleep, and it is best to repeat the test if conditions permit a more accurate assessment.

CVD Risk Assessment

Determination of the risk of CVD in hypertensive patients is the main basis for treatment decisions. Hypertensive patients can be assessed for overall CVD risk based on BP levels, risk factors, target organ damage, and associated clinical diseases.

Assessment of risk factors

Risk factors include smoking or passive smoking, high sodium and low potassium diet, alcohol consumption, 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 obese (body mass index ≥ 28 kg/m^2), family history of premature CVD (age of onset in first-degree relatives < 50 years old), and psychological and socioeconomic factors.[1,35]

In addition to the above traditional risk factors, migraine, especially migraine with aura, is an independent risk factor for stroke and ischemic heart disease.[35] Frailty is associated with poor prognosis,[36,37] cognitive function and cardiovascular events,[38] and all-cause mortality risk.[39]

Risk factors should be regularly screened and evaluated in patients with hypertension both at the initial diagnosis and during treatment follow-up. Prognosis and medical options for elevated BP and other modifiable risk factors should be discussed with hypertensive patients.

Assessment of target organ damage

Hypertension-induced structural or functional changes in the arterial vasculature and/or the organs it supplies are referred to as hypertension-mediated target organ damage. The detection of asymptomatic subclinical target organ damage in hypertensive patients is an important part of the diagnosis and evaluation of hypertension by using relatively simple, inexpensive and easy-to-promote examination methods.

The assessment includes: (1) left ventricular hypertrophy (septal or posterior left ventricular wall thickness ≥ 11 mm or left ventricular mass index in male ≥ 115 g/m^2, female ≥ 95 g/m^2); (2) carotid intima-media thickness thickening (≥ 0.9 mm) or plaque (≥ 1.3 mm); (3) decreased estimated glomerular filtration rate (eGFR) (30–59 mL/min per 1.73 m^2) or mildly elevated serum creatinine (male: 115–133 μmol/L, female: 107–124 μmol/L); and (4) microalbuminuria (30–300 mg/24 h or albumin/creatinine ratio of 30–300 mg/g).[1] In addition, the PWV is an indicator of arterial stiffness and changes in an age-dependent manner.[40] Carotid-femoral PWV ≥ 12 m/s or brachial-ankle PWV ≥ 18 m/s can be used as a criterion for target organ damage in elderly individuals.[40-42] A patient can have multiple target organ damages.[43] The risk is higher when the damage involves multiple organs.

Target organ damage may be a rationale for providing antihypertensive therapy to middle-risk elderly patients with high normotensive values.

Concomitant diseases

Concomitant diseases include heart disease [myocardial infarction (MI), angina pectoris, coronary revascularization, congestive HF], cerebrovascular disease (ischemic stroke, cerebral hemorrhage, transient ischemic attack), DM, kidney disease (diabetic nephropathy, impaired renal function) and peripheral vascular disease.[1]

It must be considered that hypertensive patients with chronic inflammatory disease, chronic obstructive pulmo-

nary disease, and mental illness have higher CVD risk and need effective BP control.[35,44]

Hypertension Risk Stratification[1,44,45]

The overall cardiovascular risk assessment of elderly hypertensive patients is helpful to determine the timing of antihypertensive treatment, optimize treatment plans, and comprehensively cardiovascular risk management. Treatment decisions are particularly important in elderly patients aged 60–79 years with SBP of 130–139 mmHg or DBP of 85–89 mmHg. Because old age itself is a risk factor, elderly hypertensive patients are stratified to the moderate-risk group with at least (Table 6).

Frailty Assessment

Elderly hypertensive patients with reduced physical activity and very old hypertensive patients should be routinely assessed for frailty.

The main feature of the coexisting debilitating state in elderly hypertensive patients is that the physiological reserves of multiple organs, such as cardiovascular, neuromuscular, metabolic and immune systems, are reduced, which leads to the weakening of the elderly's individual's ability to adapt to fluctuations in BP and physiological metabolism, resisting external stressors and maintaining the perfusion of vital organs and tissues and stabilization of the internal environment, which is likely to cause adverse clinical outcomes.[46] The 6-m walking test, frailty index, FRAIL scale or FRIED evaluation criteria are usually used to assess diseases and multiple organ functions, nutritional status, weight changes, and subjective experiences of fatigue.[47-49] The maintenance and promotion of patients' quality of life and functional preservation should be adopted as the fundamental management goals,[50,51] based on the evaluation results, to determine the appropriate antihypertensive strategies for elderly patients, including the timing of antihypertensive initiation, antihypertensive target, and optimized drug regimens. At present, most international guidelines recommend actively conducting a comprehensive geriatric assessment (CGA) or assessment of the degree of frailty in elderly hypertensive patients with frailty, appropriately relaxing the BP level of initial treatment and BP target prudently carrying out antihypertensive therapy, and monitoring of drug interactions and adverse reactions.[50-53]

The FRAIL scale and FRIED criteria are shown in Table 7[54] and Table 8[54,55]:

Assessment of Cognitive Function

Mild cognitive impairment (MCI, a precursor to dementia) and dementia are important problems affecting the quality of life of elderly people and increasing their long-

Table 6 Risk stratification of elderly hypertensive patients.

Other risk factors and medical history	Blood pressure level			
	SBP 130–139 mmHg and/or DBP 85–89 mmHg	SBP 140–159 mmHg and/or DBP 90–99 mmHg	SBP 160–179 mmHg and/or DBP 100–109 mmHg	SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg
1–2 risk factors	moderate risk	moderate risk	high risk	very high risk
≥ 3 risk factors or target organ damage or CKD stage 3 or diabetes mellitus	high risk	high risk	very high risk	very high risk
Concomitant clinical conditions, CKD stage 4 to 5	very high risk	very high risk	very high risk	very high risk

CKD: chronic kidney disease; DBP: diastolic blood pressure; SBP: systolic blood pressure.

Table 7 FRAIL scale.

Serial number	Items	Query
1	Fatigue	You fell tired all or most of the time during the past 4 week
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 mellitus, 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 criteria.

Serial number	Test item	Male	Female
1	Loss of weight	Unintentional weight loss [10 pounds (4.5 kg) or > 5%] in past year	
2	Walking time, 4.57 m	Height ≤ 173 cm: ≥ 7 s Height > 173 cm: ≥ 6 s	Height ≤ 159 cm: ≥ 7 s Height > 159 cm: ≥ 6 s
3	Grip strength, kg	BMI ≤ 24.0 kg/m^2: ≤ 29 kg BMI 24.1–26.0 kg/m^2: ≤ 30 kg BMI 26.1–28.0 kg/m^2: ≤ 30 kg BMI > 28.0 kg/m^2: ≤ 32 kg	BMI ≤ 23.0 kg/m^2: ≤ 17 kg BMI 23.1–26.0 kg/m^2: ≤ 17.3 kg BMI 26.1–29.0 kg/m^2: ≤ 18 kg BMI > 29.0 kg/m^2: ≤ 21 kg
4	Physical activity, MLTA	< 383 kcal/week (Approx. 2.5 h of walking)	< 270 kcal/week (Approx. 2 h of walking)
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 Physical Activity.

term mortality. In hypertensive patients, MCI is very common, accounting for approximately 30%.[56] In a cross-sectional study of low-income people over 60 years old in northern China, the prevalence of MCI was significantly higher in hypertensive patients, especially in patients with grade 3 hypertension.[57] A national epidemiological survey from 2015 to 2018 published in China in 2020 found that the risk of dementia and MCI in hypertensive patients increased by 1.86 times and 1.62 times, respectively.[58] High BP impairs cognitive performance across the lifespan, increasing the risk of early-onset and late-stage dementia.[59] Its mechanism involves changes in cerebrovascular structure and function caused by long-term hypertension,[60] leading to vascular endothelial injury, decreased cerebral blood perfusion, destruction of the blood–brain barrier, increased deposition of beta-amyloid in the brain and other conditions.[61,62]

Since 2018, the World Health Organization has recommended that lowering the BP can reduce the risk of cognitive decline and dementia.[63] A meta-analysis in 2020 showed that in hypertensive patients, those receiving antihypertensive treatment could reduce the risk of dementia by 12 percent and Alzheimer's disease by 16 percent compared with those who did not receive treatment, and this effect was not significantly different among treatments with angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), beta-blockers, calcium channel blockers (CCBs) and diuretics.[64] It is recommended to give antihypertensive treatment to elderly patients with cognitive impairment, but attention should be paied to adjust the dosage of drugs so as to avido BP significantly lower than the target value.

Attention should be given to early screening of cognitive decline in elderly hypertensive patients, and it is recommended to use the Ascertain Dementia 8-item Questionnaire (Table 9).[65] The cognitive function of the elderly should be quickly screened. For elderly patients with a score of ≥ 2, a comprehensive evaluation should be carried out, and they should be referred to the neurology department for comprehensive management (Figure 1). Antihypertensive therapy can be given to elderly hypertensive patients with cognitive impairment. There is no speci-

Table 9 Ascertain Dementia 8-item Questionnaire.

Serial number	Items
1	Judgment problems (cannot make up their minds, make wrong decisions, buy gifts that are not suitable for the other party's identity, or adjust their activities according to current conditions and environmental changes)
2	Loss of interest, disengagement from one's hobbies and favorite activities
3	Asking the same thing repetitively
4	Difficulty learning to use common tools, household appliances, or equipment (e.g., basic functions of washing machines, computers, microwave ovens, cameras or mobile phones)
5	Cannot remember what year and month it is
6	Difficulty dealing with complex personal financial affairs (forgetting how to reconcile accounts or purchase water, electricity, or gas; unable to manage income reasonably)
7	Cannot remember appointments with other people (such as an appointment to travel together)
8	Frequent problems with memory or thinking skills

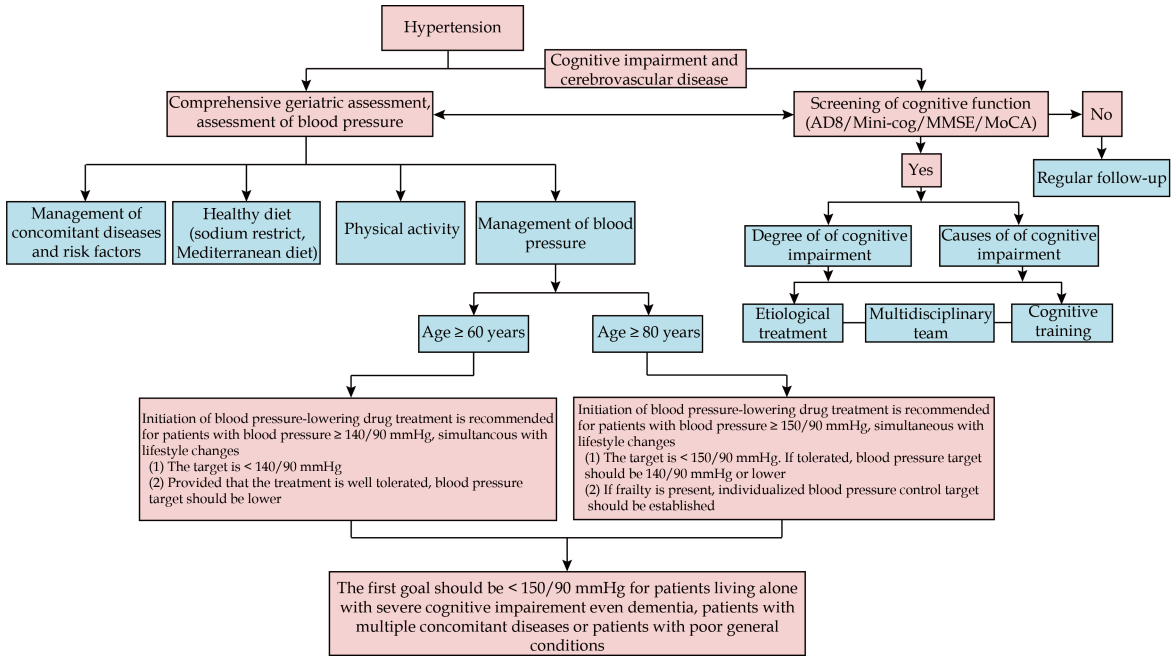

Figure 1 Flow chart of the management of hypertension complicated with cognitive impairment. AD8: Ascertain Dementia 8-item Questionnaire; Mini-cog: Mini-Mental State Intelligence Scale; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment.

al recommendation for the type of antihypertensive drugs, and the target value of antihypertensive drugs should be individualized. For patients living alone with severe cognitive impairment or even dementia, a looser BP control strategy is recommended.

TREATMENT

General

Objective of antihypertensive therapy

Through reasonable control of BP and other risk factors, the risk of damage to target organs such as the heart, brain, kidney and peripheral blood vessels and mortality and disability rate can be minimized, the quality of life of patients can be improved, and the life expectancy of patients can be prolonged.[1] The elderly patients with hypertension are mainly characterized by increased SBP, normal or even low DBP. The antihypertensive treatment of elderly hypertension should focus on the SBP reaching the target, and at the same time, excessive reduction of DBP should be avoided.

Principles of antihypertensive therapy

Compared with young and middle-aged patients, elderly hypertensive patients with frailty or cognitive impairement have a worse tolerance for BP drops, so it is necessary to start with low doses of antihypertensive drugs and strengthen the management gradually and slowly according to the patient's tolerance. Increase the intensity of treatment until the target BP is reached. While actively controlling BP, various reversible risk factors (such as dyslipidemia, abnormal glucose metabolism, smoking, obesity, etc.) should also be screened and controlled, and the related target organ damage and clinical diseases should be considered and treated. Most patients require long-term or even lifelong adherence to treatment.

Timing of antihypertensive therapy

On the basis of lifestyle intervention, most elderly hypertensive patients need to receive antihypertensive drugs to ensure that the BP reaches the target. The timing of the initiation of antihypertensive drug therapy is shown in Table 10.

Target of antihypertensive therapy

In recent years, the Systolic Blood Pressure Intervention Trial (SPRINT) has been announced successively.[66] A study of the intervention strategy of antihypertensive targets in the Elderly Hypertensive Patients (STEP) trial[67] and the Blood Pressure Lowering Treatment Trialists' Co-

Table 10 Timing of antihypertensive drug therapy initiation and blood pressure control goals.

Recommendation	Recommended category	Evidence grading
Initiation of BP-lowering drug treatment is recommended for patients aged 65–79 years and BP ≥ 140/90 mmHg, simultaneous with the initiation of lifestyle changes, the target is < 140/90 mmHg and BP target can be < 130/80 mmHg if tolerated	Class I	Level A
Initiation of BP-lowering drug treatment is recommended for patients aged ≥ 80 years and BP ≥ 150/90 mmHg	Class I	Level A
The first goal should be lowering BP to < 150/90 mmHg	Class I	Level A
BP target can be lower if well tolerated	Class IIa	Level B
Initiation of BP-lowering drug treatment is recommended for frail patients aged ≥ 80 years and BP ≥ 150/90 mmHg. The systolic BP target is 130–150 mmHg, or the BP control target should be determined individually according to the actual situation of the patient	Class IIa	Level C
If the patient tolerates antihypertensive therapy well, antihypertensive therapy should continue	Class I	Level A

BP: blood pressure.

llaboration (BPLTTC) meta-analysis[68,69] showed that more stringent BP control in elderly hypertensive patients can bring more benefits. Therefore, this version of the guidelines recommends that the BP of nonfrail elderly hypertensive patients aged 65–79 years should be controlled to < 130/80 mmHg. At present, the Hypertension in the Very Elderly Trial (HYVET) study is the only large randomized controlled trial specifically for elderly hypertensive patients ≥ 80 years old; it confirmed that the SBP of elderly hypertensive patients should be controlled below 150 mmHg, which is not only safe but also provides significant clinical benefits.[70] Therefore, this guide recommends < 150/90 mmHg as a BP target for nonfrail elderly patients, and a lower BP control target can be tried under the premise of good tolerance. The efficacy and safety of stricter BP control in patients over 80 years old and in frail elderly individuals are still not fully demonstrated. Therefore, this edition recommends an individualized BP management strategy, and clinicians should determine the appropriate BP according to patient tolerance. However, SBPs < 130 mmHg should be avoided.[53]

Lifestyle Interventions

Lifestyle intervention is the basic foundation of antihypertensive treatment,[71] mainly including a healthy diet, smoking cessation and limitation of alcohol consumption, maintaining an ideal body weight, engaging in reasonable exercise, improving sleep, keeping warm and attaining a psychological balance.

Healthy diet

Sodium restrict and potassium-rich diet may help the patients control the BP.[72,73] The World Health Organization recommends sodium intake < 5 g/d. Elderly hypertensive patients should moderately limit salt and reduce cooking salt and soy sauce and other condiments with a high sodium content. It is recommended that people with normal renal function choose low-sodium and potassium-rich foods instead of salt. The elderly population should be encouraged to consume a variety of fresh vegetables, fruits, fish, soy products, whole grains, skim milk and other foods rich in potassium, calcium, dietary fiber, and polyunsaturated fatty acids.

Smoking and alcohol cessation

Smoking cessation reduces the risk of CVD, lung disease and death.[74] It is recommended that elderly smokers quit smoking, apply smoking cessation drugs if necessary to reduce withdrawal symptoms, increase the success rate of smoking cessation, and avoid using e-cigarettes instead.[75] Drinking alcohol increases the risk of high BP,[76,77] and moderate-to-heavy drinkers who limit alcohol consumption can significantly lower BP.[78] Older adults are advised to limit alcohol intake, with a daily alcohol intake of < 25 g in men and < 15 g in women. The intake of liquor, wine (or rice wine), and beer should be < 50 mL/d, 100 mL/d and 300 mL/d, respectively.

Maintain ideal body weight

Overweight or obese elderly hypertensive patients can appropriately control their caloric intake and do more physical activity to reduce BP through weight loss.[79] Maintaining ideal body weight (body mass index: 20.0–23.9 kg/m^2) and rectifying abdominal obesity (abdominal circumference: male ≥ 90 cm, female ≥ 85 cm) are beneficial for controlling BP and reducing the risk of CVD, but the elderly should pay attention to avoid rapid or excessive weight loss.

Reasonable exercise

Reasonable aerobic exercise can effectively reduce BP in elderly patients with hypertension and prehypertension.[80] Resistance exercise can also increase muscle strength and prevent and improve aging.[81] It is recommended that the elderly engage in appropriate regular exercise, such as walking, jogging, swimming, etc., no less than 5 days a week and for no less than 30 min a day. Such activities should mainly involve moderate-intensity aerobic exercise, combined with resistance exercise, balance training, breathing training, flexibility and stretching training. Strenuous exercise is not recommended for elderly individuals.

Sleep improvement

The duration and quality of sleep are associated with the increase of BP and risk of CVD.[82] Guaranteeing 6–8 h of adequate nighttime sleep and improving sleep quality are of great significance for improving quality of life, controlling BP and reducing complications of cardiovascular and cerebrovascular diseases. The elderly should not sleep too long during day-time and diuretics should be avoided to take before going to bed, so as not to affect sleep with excessive urine at night.

Keeping warm

BP changes with the seasons; typically, the office SBP/DBP in winter is on average approximately 5/3 mmHg higher than that in summer.[83] Elderly individuals have a poor ability to adapt to cold and regulate BP and often have obvious seasonal BP fluctuations. Elderly patients should keep the room warm, ventilate frequently, reduce times of going out during sudden cold and strong wind and low temperature, add appropriate clothing, and keep warm to avoid large fluctuations in BP.

Psychological balance

Elderly individuals should develop a mentality of not being alarmed and not panicking and avoiding events that will cause their emotions to fluctuate.

Pharmacological Therapy

Basic principles of pharmacological therapy for the elderly

The following principles should be followed when we treat elderly patients with hypertension: (1) low dose: a low effective therapeutic dose is usually used for the initial treatment of elderly, frail or cognitively impaired hypertensive patients, and gradually increase the dose as needed; (2) long-acting: as far as possible, we should use long-acting and 24 h effective antihypertensive drugs that could be administrated once a day to effectively control nighttime BP, morning BP peaks and cardiovascular and cerebrovascular complications; (3) combination: if the effect of single drug treatment is unsatisfactory, two or more low-dose antihypertensive drugs can be used in combination therapy to increase the antihypertensive effect, and single-pill combination are preferred; and (4) individualization: according to the specific situation of the patient (especially frail elderly individuals and the older population over 80 years old), tolerance, personal wishes and long-term tolerance, antihypertensive drugs suitable for the patient should be selected.

Types and characteristics of commonly used antihypertensive drugs

Commonly used antihypertensive drugs include CCBs, ACEIs, ARBs, diuretics, beta-blockers. Other types of antihypertensive drugs can sometimes be used in certain specific populations (Table 11).

Taking the risk factors, subclinical target organ damage and concomitant clinical diseases of patients into consideration a certain type of antihypertensive drug is preferred[84-88] (Tables 12 & 13). These antihypertensive drugs were as follows: (1) 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; (2) ACEIs: ACEIs have a favorable effect on target organ protection and cardiovascular endpoint event prevention, especially for the elderly hypertensive patients with chronic HF and MI. 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;[85] (3) ARBs: ARBs can reduce proteinuria and microalbuminuria in patients with DM or nephropathy,[15,16] especially in patients with left ventricular hypertrophy, HF, diabetic nephropathy, metabolic syndrome, microalbuminuria or proteinuria, and patients who cannot tolerate ACEIs. The hi-

Table 11 Various commonly used antihypertensive drugs.

Classification	Drug	Daily dose, mg/d	Frequency, time/d	Notes
CCB (dihydropyridine)	Amlodipine besylate	2.5–10	1	No absolute contraindication Dose-related ankle edema, flushing and constipation were more common in females than in males The side effects of levamlodipine like ankle edema were relatively few
	Levoamlodipine	1.25–5	1	
	Felodipine extended release	2.5–10	1	
	Cilnidipine	5–10	1	
	Lercanidipine	10–20	1	
	Nifedipine sustained release	10–80	2	
	Nifedipine controlled release	30–60	1	
	Lacidipine	4–8	1	
	Benidipine	4–8	1	
CCB (non-dihydropyridine)	Diltiazem zaozi001 extended release	90–360	1–2	Avoid routine combination with beta-blockers for the potential of bradycardia and conduction block
	Verapamil extended release	120–240	1	Not suitable for systolic heart failure
ACEI	Benazepril	5–40	1–2	The combination of ACEI and ARB is not recommended ARB is an altered choice for patients with dry cough who cannot tolerate ACEI Patients with chronic kidney disease or using potassium supplements or potassium-preserving drugs increase the risk of high potassium Risk of acute renal failure increased in patients with severe bilateral renal artery stenosis The ACEIs are contraindicated in patients with previous angioedema associated with ACE inhibitor therapy The ACEIs are contraindicated in patients with serum creatinine > 3 mg/dL (1 mg/dL = 88.4 μmol/L)
	Captopril	25–300	2–3	
	Enalapril	2.5–40	1–2	
	Fosinopril	10–40	1	
	Lisinopril	2.5–40	1	
	Imidapril	2.5–10	1	
	Perindopril	4–8	1	
	Ramipril	1.25–10	1	
ARB	Candesartan	4–32	1	Precautions are the same as ACEI
	Irbesartan	150–300	1	
	Losartan	25–100	1	
	Olmesartan	20–40	1	
	Telmisartan	20–80	1	
	Valsartan	80–160	1	
	Azilsartan	40–80	1	
Thiazide diuretics	Hydrochlorothiazide	6.25–25	1	Sodium, potassium, uric acid and calcium concentrations should be monitored
Thiazide-like diuretics	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

Continued

Classification	Drug	Daily dose, mg/d	Frequency, time/d	Notes
Loop diuretics	Bumetanide	0.5–4	2	For patients with symptomatic heart failure, loop diuretics are preferred For patients with moderate to severe chronic kidney disease, loop diuretics are preferred
	Furosemide	20–80	2	
	Torasemide	5–10	1	
Potassium-sparing diuretics	Amiloride	2.5–10	1–2	The antihypertensive effect of single use was not obvious Avoid these drugs in patients with severe chronic kidney disease
	Triamterene	25–100	1–2	
Aldosterone receptor antagonist	Eplerenone	50–100	2	Spironolactone increases the risk of gynecomastia and erectile dysfunction Avoid combined use of potassium supplements and potassium-sparing drugs Avoid use in patients with severe chronic kidney disease
	Spironolactone	20–80	Take in divided doses	
Cardioselective beta-receptor antagonists	Metoprolol succinate	47.5–95	1	Beta-blockers are contraindicated in patients with disease of bronchospasm When beta-blockers must be used, highly beta1-selective beta blockers could be selected Avoid abrupt withdrawal
	Metoprolol tartrate	50–100	2	
	Bisoprolol	2.5–10	1	
	Atenolol	12.5–50	1–2	
Alpha- and beta-receptor antagonists	Carvedilol	12.5–50	2	
	Arotinolol	10–20	1–2	
	Labetalol	200–600	2	
	Bevantolol	100–200	1–2	
Angiotensin receptor/neprilysin inhibitor	Sacubitril/Valsartan	50–200	1–2	Cannot be used in combination with ACEI, ARB, or aliskiren. If switching from ACEI to angiotensin receptor-neprilysin inhibitor, stop ACEI treatment for at least 36 h to start the application
Alpha-receptor blockers	Doxazosin	1–16	1	Those drugs may cause postural hypotension, particularly in the elderly patients Alpha1-receptor antagonism can be used as second-line drug for the patients with benign prostatic hyperplasia
	Prazosin	2–20	2–3	
	Terazosin	1–20	1–2	
Central antihypertensive drugs	Clonidine	0.1–0.8	2	Avoid abrupt withdrawal in case of hypertensive crisis
	Methyldopa	250–1000	2	
	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.

Table 12 Selection of antihypertensive drugs for the elderly population.

Recommendation	Recommended category	Evidence grading
It is recommended to use thiazide/like diuretics, CCB, ACEI/ARB/ARNI for the initiation and maintenance of antihypertensive therapy, either single or in combination	Class I	Level A
For nonfrail hypertensive patients aged 65–79 years with grade 2 or higher hypertension or blood pressure higher than target blood pressure 20/10 mmHg, two-drug combination therapy can be used for initial and maintenance treatment, and single-pill combination agents are preferred to improve treatment compliance	Class I	Level B
ACEI, ARB and ARNI should not be used in combination	Class III	Level A

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor-neprilysin inhibitor; CCB: calcium channel blocker.

Table 13 Preferred drugs for elderly hypertensive patients in certain clinical condition.

Clinical conditions	Drugs
Asymptomatic target organ damage	
Left ventricular wall hypertrophy	ACEI, ARB, CCB, ARNI
Asymptomatic atherosclerosis	ACEI, ARB, CCB
Microalbuminuria	ACEI, ARB
Mild renal insufficiency	ACEI, ARB, ARNI
Clinical cardiovascular events	
Previous myocardial infarction	Beta-blocker, ACEI, ARB
Angina pectoris	Beta-blocker, CCB
Heart failure	Diuretics, beta-blockers, ACEI, ARB, aldosterone receptor blocker, ARNI
Aortic aneurysm	Beta-blockers, ARB
Atrial fibrillation, prevention	ACEI, ARB, beta-blockers, aldosterone antagonist
Atrial fibrillation, ventricular rate control	Beta-blockers, non-dihydropyridine CCB
Kidney damage, proteinuria	ACEI, ARB, ARNI
Peripheral arterial diseases	ACEI, ARB, CCB
Other	
Isolated systolic hypertension (geriatric)	Diuretics, CCB
Metabolic syndrome	ACEI, ARB, CCB
Diabetes mellitus	ACEI, ARB
Benign prostatic hyperplasia	Alpha-blockers

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor-neprilysin inhibitor; CCB: calcium channel blocker.

gher the selectivity, the stronger the affinity, and the longer the binding time of ARB binding to the angiotensin II type 1 receptor, the stronger is its blocking effect on the angiotensin II type 1 receptor, and the more significant the antihypertensive effect;[89] (4) Diuretics: diuretics are commonly used antihypertensive drugs in elderly hypertensive patients, and low doses are recommended to reduce adverse reactions. (a) Thiazide diuretics: according to the molecular structure, these drugs can be divided into thiazide-type diuretics (such as hydrochlorothiazide) and thiazide-like diuretics (such as indapamide). (b) Potassium-sparing diuretics: these are a type of aldosterone receptor antagonists, steroidal aldosterone receptor blockers, represented by spironolactone and eplerenone. Pharmacological effects of another type is independent of aldosterone, and representative drugs include triamterene and amiloride. Diuretics are especially suitable for elderly patients with hypertension, refractory hypertension, HF combined with hypertension and salt-sensitive hypertension; (5) Beta-blockers: beta-blockers are suitable for elderly hypertensive patients with tachyarrhythmia, angina pectoris, and chronic HF. In studies comparing other antihypertensive drugs, beta-blockers did not show an advantage in reducing the incidence of stroke events;[90,91] (6) Angiotensin receptor-neprilysin inhibitor (ARNI): sacubitril, the neprilysin inhibitor, can inhibit the degradation of

natriuretic peptides by enkephalinase and exert diuretic, natriuretic, vasodilatory, and antisympathetic effects. ARB can avoid the compensatory activation of the renin-angiotensin system after enkephalinase inhibition, and play a synergistic antihypertensive effect. The combination of the two forms ensures the synchronization of the efficacy of the drugs. This is especially suitable for elderly hypertensive patients with HF and CKD;[88] and (7) Alpha-blockers: alpha-blockers have no obvious effect on glucose and lipid metabolism and can be used for elderly patients with DM, hyperlipidemia, peripheral vascular disease, asthma, benign prostatic hypertrophy, or combined treatment with multiple drugs and can also be used for treatment of refractory hypertension.

Combination of antihypertensive drugs

For elderly hypertensive patients whose BP is not up to standard on monotherapy, combination of two antihypertensive drugs can be used.[70,92-103] Combination therapy may start with low-dose regimen and if the BP is not well controlled, it can be gradually adjusted to the standard dose. When used in combination, the antihypertensive mechanisms of the drugs may be complementary and can offset or reduce adverse drug reactions, such as ACEIs, ARBs or ARNI combined with low-dose thiazide diuretics. The combination of antihypertensive drugs with similar mechanisms of action, such as ACEIs, ARBs, and ARNIs, should be avoided.[88,104,105] However, thiazide/loop diuretics and potassium-sparing diuretics can be used in combination in certain conditions (e.g., hypertension with HF), as could dihydropyridine CCBs and non-dihydropyridine CCBs. For patients with high-normal BPs who need drug treatment and grade 1 hypertension, the use of Chinese patent medicines with evidence-based functions such as calming the liver and suppressing yang can be considered to assist in BP or as a combination of commonly used antihypertensive drugs to control BP and improve BP-related symptoms.[106,107]

When a three-drug combination is needed, the combination regimen consisting of dihydropyridine CCB, ACEI/ARB, and thiazide diuretics is the most commonly used. For patients with refractory hypertension, a fourth drug, such as beta-blockers, spironolactone, or alpha-blockers, can be added to the abovementioned three-drug combination.

Fixed-dosed single-pill combination agents usually consist of antihypertensive drugs with different mechanisms. Compared with free combination antihypertensive therapy, single-pill combination agents are more convenient, thus compliance in elderly patients may be improved.[108] The current evidence is in favor of recommending single-tablet combination preparations for initial and long-term maintenance therapy. For elderly patients aged 65–79 years without frailty whose BP is higher than the target value of 20/10 mmHg, the routine doses can be initiated and maintained. And for the elderly patients with BP higher than the target value of 20/10 mmHg, without frail, or over 80 years old, single drug treatment is not ideal; when combined treatment is needed, single-pill combination agents are recommended.[108-113] At present, the single-pill compound combination agents listed in China mainly include ACEI + thiazide diuretics, ARB + thiazide diuretics, dihydropyridine CCB + ACEI, dihydropyridine CCB + ARB, dihydropyridine CCB + beta receptor blockers, thiazide diuretics + potassium-sparing diuretics, and traditional low-dose multicomponent combination agents. Compound reserpine triamteridine are a classic combination agent in China. The four components are synergistic, safe and effective, with good suitability and accessibility. This can also be used as a basic drug choice for patients with hypertension[114-116] (Table 14).

Follow-up after antihypertensive drug treatment

After initiation of antihypertensive drug therapy or adjustment of the drug therapy regimen in elderly hypertensive patients, monthly follow-up is required to monitor and evaluate the safety and effect of drug therapy until the BP target is reached. Follow-up contents include BP compliance, orthostatic hypotension, adverse drug reactions, treatment compliance, lifestyle changes, and the necessity of drug adjustment. Laboratory tests include electrolytes, blood glucose, blood lipids, liver and kidney function, and related target organ damage.[117-119] While taking blood lipid-regulating drugs, the level of creatinase should be regularly detected. After the initiation of antihypertensive drug treatment, the application of home BP measurement, the help of family members, and the use of telemedicine equipment can improve the BP controlled rate in elderly patients.[120-126]

ANTIHYPERTENSIVE THERAPY IN SPECIFIC CLINICAL CONDITIONS OF THE ELDERLY

Hypertension in Very Old Patient

Hypertension in patients aged ≥ 80 years is called hype-

Table 14 Common types of single-piece combination agents.

Classification	Name	Ingredient dose	Dosage
A + C	Perindopril/Amlodipine	Arginine perindopril 10 mg/Amlodipine besylate 5 mg	0.5–1 capsule, once a day
	Amlodipine/Benazepril	Amlodipine 5 mg/Benazepril 10 mg	0.5–2 capsule, once a day
		Amlodipine 2.5 mg/Benazepril 10 mg	0.5–4 capsule, once a day
	Amlodipine/Losartan	Amlodipine 5 mg/Losartan 100 mg	0.5–1 capsule, once a day
		Amlodipine 5 mg/Losartan 50 mg	0.5–2 capsule, once a day
	Olmesartan/Amlodipine	Olmesartan 20 mg/Amlodipine 5 mg	0.5–2 capsule, once a day
	Irbesartan/Amlodipine	Irbesartan 100 mg/Amlodipine 5 mg	0.5–2 capsule, once a day
		Irbesartan 100 mg/Amlodipine 10 mg	0.5–1 capsule, once a day
	Amlodipine/Valsartan	Amlodipine 5 mg/Valsartan 80 mg	0.5–2 capsule, once a day
	Amlodipine/Telmisartan	Amlodipine 5 mg/Telmisartan 80 mg	0.5–1 capsule, once a day
A + D	Perindopril/Indapamide	Perindopril 4 mg/Indapamide 1.25 mg	0.5–2 capsule, once a day
	Lisinopril/Hydrochlorothiazide	Lisinopril 10 mg/Hydrochlorothiazide 12.5 mg	0.5–2 capsule, once a day
	Benazepril/Hydrochlorothiazide	Benazepril 10 mg/Hydrochlorothiazide 12.5 mg	0.5–2 capsule, once a day
	Losartan Potassium/Hydrochlorothiazide	Losartan Potassium 50 mg/Hydrochlorothiazide 12.5 mg	0.5–2 capsule, once a day
		Losartan Potassium 100 mg/Hydrochlorothiazide 12.5 mg	0.5–1 capsule, once a day
		Losartan Potassium 100 mg/Hydrochlorothiazide 25 mg	0.5–1 capsule, once a day
	Valsartan/Hydrochlorothiazide	Valsartan 80 mg/Hydrochlorothiazide 12.5 mg	0.5–2 capsule, once a day
	Irbesartan/Hydrochlorothiazide	Irbesartan 150 mg/Hydrochlorothiazide 12.5 mg	0.5–2 capsule, once a day
	Telmisartan/Hydrochlorothiazide	Telmisartan 40 mg/Hydrochlorothiazide 12.5 mg	0.5–2 capsule, once a day
		Telmisartan 80 mg/Hydrochlorothiazide 12.5 mg	0.5–1 capsule, once a day
	Olmesartan/Hydrochlorothiazide	Olmesartan 20 mg/Hydrochlorothiazide 12.5 mg	0.5–2 capsule, once a day
	Candesartan/Hydrochlorothiazide	Candesartan ester 16 mg/Hydrochlorothiazide 12.5 mg	0.5–1 capsule, once a day
B + C	Bisoprolol/Amlodipine	Bisoprolol 5 mg/Amlodipine 5 mg	0.5–2 capsule, once a day
	Nitrendipine and Atenolol Tablets	Nitrendipine 10 mg/Atenolol 20 mg	1 capsule, once or twice a day
Compound diuretics	Compound/Amiloride	Amiloride 2.5 mg/Hydrochlorothiazide 25 mg	0.5–1 capsule, once a day
Low-dose multicomponent combination agents	Compound Reserpine/Triamteridine Tablets	Reserpine 0.1 mg/Triamterene 12.5 mg/Hydrochlorothiazide 12.5 mg/Dihydralazine 12.5 mg	0.5–1 capsule, once a day

rtension in very old patients. Lifestyle changes (such as dietary salt restriction and weight loss in obese patients) can reduce BP in elderly hypertensive patients.[127] Elderly hypertensive patients should start drug therapy if lifestyle changes are ineffective.[128] It is recommended that elderly individuals consider the treatment plan in combination with comorbidities that may affect life expectancy and the actual expectation of clinical benefit.[129] In addition, for elderly patients who are receiving antihypertensive treatment, the original treatment can continue until the age of 80 years old.[130]

The purpose of antihypertensive treatment in very old hypertensive patients is to maintain their organ function, improve quality of life and reduce total mortality, and a hierarchical and staged treatment plan should be adopted. The selection of antihypertensive drugs should follow the following principles: (1) a low dose is used as the initial treatment. If the BP is not up to the target with single drug treatment, a low-dose combination drug is recommended, and the BP should be gradually lowered to the target level within 2 to 4 months;[103,131] avoid the risk of ischemia of important organs such as the heart, brain and kidney as much as possible; (2) the choice of antihypertensive drugs should first consider its effect on the magnitude of the BP drop.[132] There are 4 classes of drugs that can be considered first-line treatment in elderly hypertensive patients: diuretics, long-acting CCBs, ACEIs or ARBs;[133] and (3) frailty and orthostatic hypotension needs to be considered dur-

ing antihypertensive therapy in the elderly population.[36] It has been reported in domestic and abroad that the proportion of hypertension in very old combined with prefrailty or frailty is as high as 74.4% to 83.4%.[36,134] Special attention should be given to orthostatic hypotension in the frail population during antihypertensive therapy to prevent an increased risk of falls.[36,135] If the patient has a higher risk of falling, the type or dose of antihypertensive drugs can be reduced as appropriate.[134]

If the BP of elderly hypertensive patients exceeds 150/90 mmHg after a lifestyle intervention, the initiation of antihypertensive therapy can be considered, and clinical evaluation of frailty and comorbidities in the elderly is necessary. Generally, step-down pressure reduction is adopted, and the initial target is lowered to < 150/90 mmHg; if tolerated, the target is further reduced to < 130–140/80–90 mmHg.[130,136-138]

Hypertension with Stroke

Antihypertensive therapy is essential and appropriate for elderly stroke patients. Lowering the BP helps reduce the risk of recurrent stroke, but BP drops that are too low or that fluctuate may affect cerebral blood perfusion. Therefore, the type and dose of antihypertensive drugs and the target value of antihypertensive drugs should be individualized, and drugs, stroke characteristics and individual conditions of the patients should be comprehensively considered.[139] The recommendations for antihypertensive treatment for elderly hypertensive patients with stroke is shown in Table 15.

Hypertension with CHD

Individualized treatment strategies should be adopted for hypertensive patients with CHD. 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.

For patients with stable angina pectoris and/or previous history of MI, beta-blockers and renin-angiotensin system 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. When angina pectoris is attacked, nitroglycerin, instant-effect Suxiao Jiuxin Pills and compound Danshen Dripping Pills can be taken sublingual. Long-acting dihydropyridine CCB can also be used as an initial treatment for patients with stable angina pectoris without a history of MI and HF. Initial antihypertensive therapy should include beta-blockers and renin-angiotensin system inhibitors in patients with acute coronary syndrome without contraindications. If BP is difficult to control or beta-blockers are contraindicated, long-acting dihydropyridine CCB could be a choice; when there is evidence of HF or pulmonary

Table 15 Recommendations for antihypertensive treatment for elderly hypertensive patients with stroke.

Recommendation	Recommended category	Evidence grading
For patients with acute ischemic stroke who have not received intravenous thrombolysis or mechanical thrombectomy, antihypertensive therapy should be initiated when blood pressure is ≥ 220/120 mmHg[140-142]	Class IIb	Level C
For patients with acute ischemic stroke who plan to receive intravenous thrombolysis or mechanical thrombectomy, blood pressure should be lowered to ≤ 185/110 mmHg[143-145]	Class IIb	Level C
For acute ischemic stroke patients treated with mechanical thrombectomy, it should be avoided to lower postoperative systolic blood pressure < 120 mmHg[146]	Class IIa	Level B
Patients with ischemic stroke or transient ischemic attack with a history of hypertension and long-term medication, if there is no absolute contraindication, the antihypertensive treatment can be restarted after a few days of onset if the condition is stable. The recommended blood pressure control target value is < 130/80 mmHg to prevent recurrence of stroke[147]	Class I	Level A
For patients with ischemic stroke or transient ischemic attack caused by intracranial large artery stenosis (70%–99%), it is recommended to control the blood pressure at below 140/90 mmHg if tolerated[148,149]	Class II	Level B
For patients with stroke or transient ischemic attack caused by low hemodynamic, the impact of the rate and magnitude of blood pressure reduction on patient tolerance and hemodynamics should be weighed	Class IIa	Level C
For patients with hypertension complicated with spontaneous cerebral hemorrhage, a stable and continuous antihypertensive strategy should be adopted to a 140 mmHg target blood pressure, and controlling the systolic blood pressure to 130–150 mmHg may be reasonable[150-154]	Class IIb	Level C

congestion, non-dihydropyridine CCB should not be given. If there is severe hypertension or persistent myocardial ischemia, intravenous beta-blockers (esmolol, etc.) can be used. Intravenous nitrates can be used to control BP and relieve symptoms of myocardial ischemia and pulmonary congestion. If accompanied by MI, HF or DM and poor BP control, aldosterone receptor antagonists could be added.[112] The recommendations for elderly hypertensive patients with CHD are shown in Table 16.

Hypertension with HF

Hypertension is one of the common causes of hospitalization in HF patients, and the proportion of patients with HF with preserved ejection fraction (HFpEF) complicated with hypertension is higher.[158] Approximately two-thirds of patients with HF have a history of hypertension.[159] Long-term elevated BP and increased left ventricular afterload promote myocardial cell hypertrophy and injury, resulting in excessive activation of the renin-angiotensin-aldosterone system and the sympathetic nervous system. The abovementioned effects persist in elderly patients and are mutually causal, resulting in ventricular remodeling and ultimately HF. Recommendations for elderly hypertensive patients with HF with reduced ejection fraction are shown in Table 17.

For elderly hypertensive patients with HF with mildly reduced ejection fraction or HFpEF, the optimal drug treatment is temporarily uncertain. The treatment strategy of HF with reduced ejection fraction can be considered, and ARNI can be considered instead of ACEI/ARB for elderly individuals. Treatment of hypertension combined with HFpEF achieves the purpose of BP reduction, organ protection and reducing HF events.[53,163] The use of sodium-glucose cotransporter 2 inhibitors reduces composite cardiovascular death events or first hospitalization for HF in patients with HF with mildly reduced ejection fraction or HFpEF, regardless of type 2 DM (Class I, Level A).[164,165] Sodium-glucose cotransporter 2 inhibitors do not have meaningful effects on SBP when used in HFpEF.[166] Therefore, there is no need to adjust the use of the original antihypertensive drugs.

For elderly hypertensive patients with symptoms of HF or edema, if HF symptoms or poor BP control are present, diuretics can be considered to reduce fluid retention. Loop diuretics are preferred in patients with significant fluid retention. Thiazide diuretics are only indicated for HF patients with mild fluid retention, hypertension and normal renal function.[167] Loop diuretics can be used in combination with aldosterone receptor antagonists. If hypokalemia and hypomagnesemia occur due to poor food intake due to gastrointestinal congestion or potassium-wasting diuretics in elderly hypertensive patients with HF,

Table 16 Recommendations for elderly hypertensive patients with coronary heart disease.

Recommendations	Recommended category	Evidence grading
For patients aged < 80 years, it is recommended to target blood pressure to < 140/90 mmHg[1,44,155,156]	Class I	Level A
If the general condition is good and the antihypertensive therapy can be tolerated, the blood pressure can be lowered to < 130/80 mmHg[44,66,157]	Class IIa	Level C
For patients aged ≥ 80 years, the blood pressure target is < 150/90 mmHg and the diastolic blood pressure should not be lower than 60 mmHg[156]	Class IIb	Level C

Table 17 Recommendations for elderly patients with hypertension and heart failure with reduced ejection fraction.

Recommendations	Recommended category	Evidence grading
In elderly hypertensive patients with heart failure with reduced ejection fraction, in addition to lifestyle improvements, renin-angiotensin-aldosterone system inhibitors, beta-blockers, sodium-glucose cotransporter 2 inhibitors and aldosterone receptor antagonists can improve the long-term prognosis	Class I	Level A
Renin-angiotensin-aldosterone system inhibitors and beta-blockers should be started at low doses, increased slowly, and titrated to the target doses in the absence of contraindications and with tolerable blood pressures	Class I	Level A
If beta-blockers are contraindicated or the patient cannot tolerate the target dose for poor heart rate control, ivabradine or its combination can be used	Class IIa	Level B
Sodium-glucose cotransporter 2 inhibitors have a certain antihypertensive effect in patients with volume-dependent hypertension[160]	Class IIa	Level B
If further blood pressure lowering is needed, amlodipine or felodipine could be considered;[161,162] non-dihydropyridine calcium channel blocker is not recommended	Class IIa	Level B

potassium magnesium aspartate (relatively mild, potassium and magnesium supplementation), potassium citrate or potassium chloride (potassium supplementation is strong, gastrointestinal reaction) can be considered; when the ACEI/ARB/ARNI and aldosterone receptor blocker combination are used in low body mass or renal insufficiency, we should pay special attention to the risk of hyperkalemia; and test electrolytes regularly and adjust drugs timely.

For elderly hypertensive patients with previous episodes or current symptoms of HF, the BP target is < 130/80 mm Hg. To prevent the symptoms of HF in elderly hypertensive patients in the preclinical HF stage, the BP should also be controlled at or below 130/80 mmHg. For low-weight elderly patients with hypertension and HF, it is necessary to be alert to the adverse effects of hypotension, electrolyte imbalance, and even cardiovascular and cerebrovascular events in the early stage of combined drug therapy.

Hypertension with CKD

Hypertension and CKD are both common chronic diseases in elderly individuals. A long-term increase in BP can lead to renal damage, and CKD can also lead to increased BP. When both are present, the CVD morbidity and mortality will greatly increase.[168] Aggressive BP control can delay the progression of CKD in elderly patients and reduce the risk of CVD morbidity and mortality. Table 18 shows the BP targets for hypertension with CKD.

The antihypertensive drug treatment of elderly patients with hypertension and CKD should be based on the urine protein level, renal function, target organ damage and complications to formulate individualized treatment strategy. The recommendations for the selection of antihypertensive drugs for hypertension with CKD are shown in Table 19.

Hypertension with DM

Hypertension combined with abnormal glucose metabolism is very common in China. Among adult hypertensive patients, 17.4% have DM, and more than 30% have abnormal glucose metabolism. The prevalence of hypertension with abnormal glucose metabolism in the elderly increases with age.[180]

Most patients with hypertension and DM have a high or very high risk of cardiovascular, so it is recommended to control their BP at < 130/80 mmHg. It is reasonable, for frail or elderly patients who cannot tolerate aggressive BP reduction, the BP target can be set to < 150/90 mmHg. See Table 20 for the BP lowering targets of hypertension complicated with DM, and see Table 21 for the recommendation for patients with hypertension and DM.

Hypertension with AF

The prevalence of AF increases significantly with age, and the incidence of AF in people ≥ 75 years old is 4.6%.[195] AF is a common complication of hypertension, and 80% of patients with AF have hypertension.[196] AF patients aged ≥ 75 years with multiple CVDs have a more than 2-fold increased risk of death and adverse events at the 1-year follow-up.[197] A randomized clinical trial found that among hypertensive patients ≥ 75 years old, wearable devices detected new-onset AF in 5.3% of cases, and 75% of these patients subsequently received anticoagulation therapy.[198] AF screening can effectively prevent the occurrence of stroke in patients.[199] It is recommended that elderly hypertensive patients > 65 years of age undergo at least one screening test for AF, and wearable device monitoring is helpful in AF screening. Active BP control is the key to the prevention and treatment of hypertension with AF. The BP target and medication are shown in Table 22. In addition, elderly hypertensive patients need to be further ev-

Table 18 Blood pressure targets for hypertension with chronic kidney disease.

Recommendation	Recommended category	Evidence grading
If blood pressure ≥ 140/90 mmHg in hypertensive patients ≥ 65 years old with CKD, nondialysis, antihypertensive drug therapy should be intiated with lifestyle intervention; blood pressure control target is < 140/90 mmHg; for those with proteinuria, is 130/80 mmHg[169,170]	Class I	Level A
The blood pressure control target of elderly hypertensive patients with CKD hemodialysis is a predialysis office blood pressure < 160/90 mmHg[169]	Class IIa	Level C
Continuously control blood pressure < 140/90 mmHg in elderly hypertensive patients with CKD peritoneal dialysis[171]	Class IIa	Level C
The blood pressure of elderly kidney transplant recipients with hypertension should be < 130/80 mmHg[44]	Class IIa	Level C

CKD: chronic kidney disease.

Table 19 Recommendation for hypertension with chronic kidney disease.

Recommendation	Recommended category	Evidence grading
In the absence of contraindications, renin-angiotensin system inhibitors (ACEI/ARB/ARNI) are the first choice for elderly hypertensive patients with chronic kidney disease, and it is recommended to start with low doses[172,173]	Class I	Level A
Serum creatinine > 3.0 mg/dL (creatinine: 1 mg/dL = 88.4 mmol/L) will increase the incidence of adverse events (hyperkalemia, acute kidney injury), and attention should be given to the current serum potassium level and kidney function when using it for the first time or increasing the dose level	Class I	Level A
Review the changes in blood pressure, creatinine and serum potassium within 2–4 weeks. If the increase in serum creatinine is greater than 30% from the baseline value, the drug should be discontinued or the dose should be reduced	Class I	Level A
Combination of two renin-angiotensin system inhibitors is not recommended[169]	Class I	Level A
Avoid combining ACEIs or ARBs with direct renin inhibitors in elderly hypertensive patients with chronic kidney disease	Class I	Level B
Because chronic kidney disease patients often have fluid retention, diuretics are often used in the treatment of elderly hypertension complicated with chronic kidney disease. Patients with estimated glomerular filtration rate > 30 mL/min per 1.73 m^2 may consider using thiazide diuretics, patients with estimated glomerular filtration rate < 30 mL/min per 1.73 m^2 may consider using loop diuretics[174]	Class I	Level C
Patients with poor efficacy of renin-angiotensin system inhibitors alone are recommended to use CCB drugs in combination, especially for hemodialysis patients. CCBs are also recommended for patients with significant renal dysfunction and salt-sensitive hypertension[175]	Class I	Level A
Elderly kidney transplant recipients is recommended to use CCB or ARB drugs as first-line antihypertensive drugs, and kidney transplant recipients with proteinuria is recommended to use ARB as first-line drugs	Class I	Level C
Sodium-glucose cotransporter 2 inhibitors cause small reductions in systolic blood pressure and improved kidney outcomes. For elderly patients with hypertension and chronic kidney disease, the use of sodium-glucose cotransporter 2 inhibitors should be based on renal function (estimated glomerular filtration rate ≥ 25 mL/min per 1.73 m^2) and overall assessment results, regardless of whether they have diabetes mellitus[176-178]	Class I	Level A
The use of finerenone is recommended for the treatment of elderly hypertensive patients with chronic kidney disease and type 2 diabetes mellitus, in order to reduce proteinuria, delay the continuous decline of renal function, reduce the risk of end-stage renal disease and cardiovascular disease, and its incidence of hyperkalemia is lower than that of traditional aldosterone receptor blocker[179]	Class I	Level A
For patients with coronary heart disease, chronic heart failure, and elderly patients with hypertension and chronic kidney disease who need heart rate control, combination therapy with beta-blockers is recommended	Class I	Level B
In elderly patients with refractory hypertension who cannot be controlled by the combination of three drugs, it is recommended to add spironolactone or other antihypertensive drugs (alpha-blockers or beta-blockers) in the absence of contraindications. Regular monitoring of renal function and electrolytes is necessary[169]	Class I	Level B

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor-neprilysin inhibitor; CCB: calcium channel blocker.

Table 20 Blood pressure targets for hypertension and diabetes mellitus.

Recommendation	Recommended category	Evidence grading
For elderly diabetic patients, it is recommended to control the blood pressure at < 130/80 mmHg, and for frail or very old patients, the blood pressure target can be set to < 150/90 mmHg	Class I	Level B
The recommended diastolic blood pressure should not be lower than 60 mmHg	Class I	Level C

aluated for thrombosis and bleeding risk and actively given anticoagulation therapy, focusing on individualized medication. Interventional therapies such as catheter ablation of AF, pacemaker implantation/atrioventricular node ablation, and left atrial appendage occlusion may benefit some patients, but evidence is insufficient in older patients. Whether "rhythm" control or "ventricular rate" control is determined by the specific circumstance.

Refractory Hypertension in the Elderly

Refractory hypertension (RH) is defined as the failure to reduce BP to < 140/90 mmHg in a month after taking

Table 21 Recommendation for hypertension with diabetes mellitus.

Recommendation	Recommended category	Evidence grading
For hypertensive patients with diabetes mellitus, ACEI/ARB is recommended when starting antihypertensive therapy with a single drug[181-185]	Class I	Level A
Dihydropyridine CCB can be used in combination with antihypertensive drugs or for patients who cannot tolerate ACEI or ARB and ARNI therapy, and CCB treatment is especially suitable for elderly patients with isolated systolic hypertension[186]	Class I	Level B
Hypertensive people with diabetes mellitus can be treated with low-dose thiazide diuretics combined with antihypertensive drugs[70,187]	Class I	Level B
Beta-receptor antagonists are not the first choice for patients with hypertension and diabetes mellitus, but for patients with heart failure or coronary heart disease, combination with highly selective beta-receptor antagonist or both alpha-, beta-receptor antagonist may be considered	Class IIb	Level B
For hypertension with diabetes mellitus, new hypoglycemic drugs that can improve cardiovascular outcomes are recommended as first choice. For patients with atherosclerotic cardiovascular disease, pancreatic glucagon-like peptide-1 receptor agonists are recommended,[188-190] and for patients with concomitant heart failure and/or renal insufficiency or proteinuria, sodium-glucose cotransporter 2 inhibitors are recommended[191-194]	Class I	Level A

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor-neprilysin inhibitor; CCB: calcium channel blocker.

Table 22 Recommendations for hypertension with atrial fibrillation.

Recommendation	Recommended category	Evidence grading
Short-term electrocardiogram and subsequent continuous electrocardiogram monitoring are recommended for elderly hypertensive patients with palpitation[200-202]	Class I	Level B
For patients with atrial fibrillation, especially those who are receiving anticoagulant therapy, antihypertensive therapy should be actively carried out to control the blood pressure at < 140/90 mmHg[10-12,203-205]	Class IIa	Level B
Angiotensin receptor blocker and angiotensin-converting enzyme inhibitor are recommended for antihypertensive therapy to prevent new-onset atrial fibrillation and recurrence of paroxysmal atrial fibrillation[203,206,207]	Class I	Level B
Oral anticoagulant therapy is recommended for all nonvalvular atrial fibrillation with CHA_2DS_2-VASc score ≥ 2 points (male), ≥ 3 points (female) if there is no contraindications[208,209]	Class I	Level A
Radiofrequency ablation is recommended for patients with symptomatic paroxysmal atrial fibrillation for whose pharmacological therapy is ineffective[210]	Class I	Level A
Radiofrequency ablation should be considered for symptomatic patients with long-term persistent atrial fibrillation whose pharmacological therapy is ineffective	Class IIa	Level C

a three-drug regimen (including diuretics) and improvement of lifestyle or BP < 140/90 mmHg but patients require 4 antihypertensive medications.[1] The prevalence of true RH in the elderly population is 12.3%.[211]

Pseudo-RH should be excluded firstly in the diagnosis of RH in the elderly. The causes of pseudo-RH including incorrect BP measurement, white coat hypertension, pseudo-hypertension, and poor treatment compliance.[44]

For elderly patients with true RH, the following factors should be actively investigated regarding poor BP control: (1) unhealthy lifestyle; (2) drugs that affect BP; (3) secondary hypertension; and (4) other factors, such as insomnia, psychological stress, chronic pain, and environmental issues (noise, low temperature, high altitude, air pollution), etc.[212]

It is recommended that elderly RH patients should be comprehensively managed in a professional hypertension diagnosis and treatment center.[213] Interventions such as reducing sodium intake, increasing potassium intake, controlling body weight, engaging in moderate exercise, regular work and rest, quitting smoking, limiting alcohol and reducing mental stress are also suitable for RH patients. Elderly individuals should pay special attention to keeping warm.

In clinical trials for RH patients, a combination of renin-angiotensin system blockers, dihydropyridine CCBs, and diuretics is commonly used, called the A-C-D combination, but no randomized controlled studies have confirmed the clinical efficacy of this combination. The principles of drug therapy based on diuretics include the following: (1) use of the maximum tolerated dose of diuretics; (2) thiazide diuretics are the best choice; and (3) when eGFR < 30 mL/min per

1.73 m^2 and volume overload, loop diuretics is recommended.[214]When serum potassium < 4.5 mmol/L and eGFR > 45 mL/min per 1.73 m^2, low-dose spironolactone, with antihypertensive therapy is preferred.[215] Existing studies have shown that the addition of spironolactone, bisoprolol, doxazosin, amiloride or clonidine as the fourth drug can significantly reduce BP, and spironolactone has the strongest antihypertensive effect.[215,216] Elderly hypertensive men with benign prostatic hyperplasia can use alpha 1 receptor blockers.[217] Sacubitril-valsartan can be used in elderly RH patients with HF with reduced ejection fraction and/or CKD stages 3–4.[218] Renal sympathetic denervation can be used as an adjuvant therapy for elderly patients with RH.[219,220]

Hypertension Emergencies and Urgencies

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.[221] Hypertensive emergencies in the elderly population mainly include hypertensive encephalopathy, intracranial hemorrhage (cerebral hemorrhage and subarachnoid hemorrhage), cerebral infarction, acute HF, acute coronary syndrome, aortic dissection, renal damage, severe perioperative hypertension, and pheochromocytoma crisis, etc. Hypertensive urgencies refers to a markedly elevated BP without acute progressive target organ damage. Patients may have symptoms caused by significant elevated BP, such as headache, chest tightness, epistaxis, and restlessness. The degree of elevated BP is not the criterion for distinguishing emergency/urgency hypertension. It is the only differentia that whether there is newly-onset acute progressive severe target organ damage.

The first goal of antihypertensive treatment in geriatric hypertensive emergencies: reduce the BP to a safe level within 30–60 min, except for stroke and aortic dissection. The mean arterial pressure should be decreased rapidly but not by more than 25% within 1–2 h. The second goal of antihypertensive treatment: after reaching the first goal, the speed of BP reduction should be slowed and oral antihypertensive drugs should be added, and the speed of intravenous administration should be gradually slowed. The BP should be reduced to 160/100–110 mmHg within the next 2–6 h. When hypoperfusion of important organs occurs after antihypertensive treatment in the very old or frail elderly individuals, the speed of antihypertensive treatment should be appropriately slowed. The third goal of antihypertensive treatment: if the BP level of the second goal is tolerable and the clinical situation is stable, reduce the BP to normal level in following 24–48 h gradually. The time for the very old or the frail elderly to reach the BP target can be extended as appropriate. The specific antihypertensive requirements, antihypertensive targets and drug selection are shown in Table 23, and the usage, onset time, duration, adverse reactions and contraindications of some intravenous antihypertensive drugs are shown in Table 24.

For elderly patients with hypertension urgencies, it is recommended that on the basis of moderate long-acting oral antihypertensive drugs, short- and medium-acting 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.

Management of Perioperative Hypertension

Perioperative hypertension refers to SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or the BP increases more than 30% of the baseline BP during the period from the decision of the surgical treatment to almost the end of the surgical-related treatment. Perioperative hypertension occurs in approximately 25% of noncardiac major surgery and 80% of cardiac surgery patients. Hypertension in elderly patients is often complicated by target organ damage and a variety of underlying diseases, and the risk of perioperative cardiovascular adverse events is high.[225,226] For patients undergoing selective surgery, an assessment of frailty, cardiovascular risk factors, and target organ damage should be performed to optimize BP management, ensure blood perfusion of important organs, and reduce perioperative complications. The BP control target should be < 150/90 mmHg; if the hypertension is combined with DM or CKD and the treatment is well tolerated, the target level can be further reduced to < 140/90 mmHg.[1,8,227,228] Large fluctuations in perioperative BP in elderly hypertensive patients should be avoided, and it is recommended to control the fluctuation range of BP within 10% of the basal BP.[53,225]

A preoperative BP < 180/110 mmHg (mild to moderate hypertension) does not affect surgery; for a preoperative SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg, it is recommended to postpone selective surgery and actively reduce the

Table 23 Specific antihypertensive requirements, goals, and drug choices for hypertension emergencies.

Clinical situation	Specification	Initial blood pressure target	Drug choice
Hypertensive encephalopathy	Cerebral perfusion needs to be ensured while lowering blood pressure, and the systolic blood pressure should be reduced by 20% to 25% within 1 h after administration, but not by more than 50%	160–180/100–110 mmHg, gradually decrease to the normal level after stabilization	Urapidil, labetalol, nicardipine
Cerebral hemorrhage	When systolic blood pressure is more than 220 mmHg in patients with acute cerebral hemorrhage, active intravenous antihypertensive treatment is needed while the blood pressure should be closely monitored. When systolic blood pressure is more than 180 mmHg, intravenous antihypertensive treatment should be adjusted and guided by clinical manifestations	Systolic blood pressure 130–180 mmHg.[151,222,223] Actively reducing the blood pressure early and controlling the systolic blood pressure at 130–150 mmHg is probably safe and reasonable (Class IIb, Level C)[151,222,223]	Urapidil, labetalol, nicardipine
Subarachnoid hemorrhage	Prevent exacerbation of hemorrhage and excessive decrease of blood pressure, which may cause transient neurological deficits and delayed diffuse lethal cerebral vasospasm	Systolic blood pressure < 150–160 mmHg	Nicardipine, nimodipine, labetalol, or esmolol
Cerebral infarction	Generally no need for tight control of blood pressure, slightly higher blood pressure is beneficial to perfusion of ischemic area, unless blood pressure ≥ 200/120 mmHg or with heart failure, aortic dissection, hypertensive encephaloathy, etc	Initiate antihypertensive therapy when blood pressure ≥ 220/120 mmHg (Class IIb, Level C);[140-142] patients who are intended to receive intravenous thrombolysis or mechanical thrombectomy should control the blood pressure to ≤ 185/110 mmHg before treatment (Class IIb, Level C);[143-145] for patients who undergo mechanical thrombectomy, it is a void to control systolic blood pressure below 120 mmHg (Class IIa, Level B)[146]	Urapidil, labetalol, nicardipine, or sodium nitroprusside
Malignant hypertension with or without kidney damage	Avoid violent fluctuations in blood pressure, steadily reduce blood pressure, and ensure renal perfusion	< 140/90 mmHg	Urapidil, nicardipine or labetalol, diuretics, pay attention to renal function and electrolytes
Acute heart failure	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, not lower than 120/70 mmHg[224]	Combined diuretics with vasodilators, urapidil, sodium nitroprusside, or nitrates
Acute coronary syndrome	Reduce blood pressure and myocardial oxygen consumption, but do not affect the coronary perfusion pressure and coronary blood flow, and prevent reflex tachycardia	< 130/80 mmHg, diastolic blood pressure > 60 mmHg[224]	Nitroglycerin, esmolol, urapidil, or diltiazem
Aortic dissection	Under the premise of ensuring organ perfusion, the blood pressure is rapidly lowered and maintained as low as possible	Systolic blood pressure < 120 mmHg, heart rate 50–60 beats/min	Esmolol, labetalol, diltiazem, urapidil, sodium nitroprusside, or nicardipine
Pheochromocytoma crisis	Due to the short half-life of periodically released catecholamines, the blood pressure fluctuates greatly in patients, and blood pressure must be closely monitored to avoid the occurrence of hypotension	Blood pressure < 160/90 mmHg in 24 h before operation[224]	Alpha-blockers such as phentolamine and urapidil are the first choice. Sodium nitroprusside and nicardipine can also be used. If tachycardia and arrhythmia exist, beta blockers can be added to alpha-blockers

BP until it is controlled; for life-threatening emergencies, no matter how high the BP is, emergency surgery is recommended to save lives. Steps should be taken to improve vital organ function.[1,53,229-232]

CCB treatment is administered before surgery and can be maintained during the perioperative period. Long-term use of beta-blockers before surgery should not be discontinued during the perioperative period, especially when the hypertension is combined with CHD; if beta-blockers are not used before surgery, routine use is not recommended during the perioperative period.[233-237] For hypertensive patients who are taking ACEIs or ARBs without HF, it is recommended to suspend the use 24 h before surgery and restart the use as soon as possible after surgery.[53,238,239] The aim of perioperative hypertension (Table 25) is to control the BP as soon as possible, and intrave-

Table 24 The usage, onset time, duration, adverse reactions and contraindications of some commonly used intravenous antihypertensive drugs.

Drug	Dose	Onset time	Duration	Adverse reactions	Contraindications
Nitroglycerin	5–100 μg/min, i.v.	2–5 min	5–10 min	Headache, vomiting	Allergy to nitrates, severe anemia, increased intracranial pressure, angle-closure glaucoma
Sodium nitroprusside	0.25–10 μg/kg per min, i.v.	Immediately	2–10 min	Hypotension, tachycardia, headache, muscle spasm. If patients with renal insufficiency use persistently for more than 48 h, cyanide or thiocyanate in plasma must be measured every day, and thiocyanate should not exceed 100 μg/mL, cyanide does not exceed 3 μmol/mL to prevent cyanide poisoning	Compensated hypertension such as arteriovenous shunt or coarctation of the aorta
Labetalol	20–80 mg, i.v.; 0.5–2 mg/min, iv.gtt; not to exceed 300 mg in 24 h	5–10 min	3–6 h	Nausea, vomiting, headache, bronchospasm, conduction block, orthostatic hypotension	Bronchial asthma, cardiogenic shock, second- to third-degree atrioventricular block, sinus bradycardia, severe or acute heart failure
Esmolol	250–500 μg/kg, i.v.; then 50–300 μg/kg per min, iv.gtt	1–2 min	10–20 min	Hypotension, nausea	Severe sinus bradycardia, second- to third-degree atrioventricular block, sick sinus syndrome, cardiogenic shock, decompensated heart failure, bronchial asthma attack or exacerbation
Urapidil	10–50 mg, i.v.; 6–24 mg/h	5 min	2–8 h	Hypotension, dizziness, nausea, tiredness	Patients with aortic isthmus stenosis or arteriovenous shunt (except shunt during renal dialysis)
Nicardipine	0.5–10 μg/kg per min, i.v.	5–10 min	1–4 h	Tachycardia, headache, peripheral edema, nausea	Severe aortic stenosis, severe mitral stenosis, obstructive hypertrophic cardiomyopathy, hypotension, acute cardiac insufficiency with cardiogenic shock, severe acute myocardial infarction with unstable cardiac function
Diltiazem	5–10 mg, i.v.; 5–15 μg/kg per min, pump in	5 min	30 min	Bradycardia, atrioventricular block, heart failure, peripheral edema, headache, constipation, hepatotoxicity	Severe hypotension or cardiogenic shock, second- to third-degree atrioventricular block or sick sinus syndrome (persistent sinus bradycardia, sinus arrest and sinoatrial block, etc.), severe congestive heart failure, severe cardiomyopathy

Table 25 Recommendations for the management of hypertension in elderly patients during the perioperative period.

Recommendation	Recommended category	Evidence grading
For selective surgery, it is recommended to postpone the operation of patients with systolic blood pressure ≥ 180 mmHg and/or diastolic blood pressure ≥ 110 mmHg[1,53,232]	Class IIa	Level C
The perioperative blood pressure 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 blood pressure should be further reduced to less than 140/90 mmHg[1,8,226-228]	Class IIa	Level C
Perioperative blood pressure fluctuations should be controlled within 10% of the baseline blood pressure[53,225,226]	Class IIa	Level C
Long-term use of beta-blockers before surgery and continued use in the perioperative period	Class IIa	Level B
For patients who did not use beta-blockers before surgery, it is not recommended to use these drugs routinely in the perioperative period[233-237]	Class III	Level A
For patients without heart failure who are taking ACEIs or ARBs, it is recommended to temporarily stop these medications 24 h before surgery and to restart them as soon as possible after surgery[53,238]	Class IIa	Level C

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

nous antihypertensive drugs with a rapid onset and short duration of action, including sodium nitroprusside, urapidil, nicardipine, esmolol, labetalol and phentolamine, are recommended.[1]

Heart Rate Management in Elderly Hypertensive Patients

The incidence of cardiovascular events in hypertensive patients with heart rates > 80 beats/min is significantly higher than that with relatively slow heart rates.[240,241] It is suggested that the cutoff point of heart rate intervention for elderly hypertensive patients in China be defined as a resting heart rate > 80 beats/min, and the heart rate should be controlled to the target heart rate according to the corresponding guidelines. BP regulation ability is poor in elderly individuals, and mood swings, or anxiety and depression can cause rapid heart rates, BP fluctuations, and frequent atrial or ventricular premature contractions. Drugs that regulate the heart rate mainly include beta-blockers, non-dihydropyridine CCBs, and ivabradine, etc. Elderly patients with hypertension complicated by respiratory diseases or intermittent claudication of lower extremities should be given beta 1 receptor blockers (metoprolol, bisoprolol) as first choice to adjust their heart rate and avoid sudden drug withdrawal.

For ventricular arrhythmia, antiarrhythmic drugs should be selected according to hemodynamics and cardiac function status. Beta-receptor antagonists, non-dihydropyridine CCBs, and Class Ic antiarrhythmic drugs should be selected while maintaining electrolytes, especially potassium and magnesium. Patients with hypokalemia are recommended to use potassium magnesium aspartate, potassium citrate, and potassium chloride sustained-release tablets (Class IIa, Level C).[242,243] For elderly patients with frequent atrial and ventricular premature beats, evidence-based Chinese patent medicines with the functions of invigorating qi and nourishing yin, promoting blood circulation and relieving pain can also be considered as adjuvant therapy to reduce the frequency of premature beats and improve arrhythmia-related symptoms, which can be used alone or in combination with beta-blockers (Class IIb, Level C).[244]

Elderly hypertensive patients with bradyarrhythmias should first correct reversible factors such as drug overdose and hyperkalemia and avoid using drugs that slow the heart rate. Consider cardiac pacing therapy if symptomatic bradycardia still exists (such as transient amaurosis, syncope, etc.). Recommendations for heart rate management in elderly hypertensive patients are shown in Table 26.

Geriatric Hypertension Complicated with Multiple Organ Dysfunction

Hypertension in elderly patients is often complicated by cardiovascular and cerebrovascular diseases, DM, CKD and other systemic diseases, and geriatric syndromes such as frailty, sarcopenia, cognitive impairment, and malnutrition. Hypertension may be complicated with multiple organ dysfunction syndrome in elderly (MODSE), which is a critical illness in elderly hypertensive patients. Elevated and significantly fluctuating BP not only further damages the functions of important organs such as the heart, kidney and blood vessels in patients with MODSE but also significantly reduces the patient's physical function and quality of life. Significantly diminished tolerance to treatment and adverse drug reactions significantly increase the risk of organ failure and death.[252] MODSE

Table 26 Recommendations for heart rate management in elderly hypertensive patients.

Recommendation	Recommended category	Evidence grading
For patients with hypertension and coronary heart disease, the target resting heart rate is 55–60 beats/min; beta-blockers are recommended, and non-dihydropyridines CCBs can be selected for those who cannot tolerate beta-blockers or have contraindications[245,246]	Class I	Level B
For patients with hypertension and heart failure with reduced ejection fraction, the target resting heart rate is < 70 beats/min, and beta-blockers are recommended. Ivabradine is recommended for those who cannot reach the target heart rate or cannot tolerate beta-blockers[167,247]	Class IIa	Level B
Hypertension complicated with arrhythmia: the initial resting heart rate target for rapid atrial fibrillation is < 110 beats/min. If symptoms are still obvious, the heart rate can be controlled to 80–100 beats/min with beta-blockers dihydropyridine CCBs, digitalis, etc[248,249]	Class IIa	Level C
Patients with ventricular arrhythmia should receive antiarrhythmic drugs according to their hemodynamics and cardiac function status, with such drugs including beta-receptor blockers, non-dihydropyridine CCBs, and Class Ic antiarrhythmic drugs; at the same time, maintain electrolytes, especially potassium, magnesium ion balance; patients with hypokalemia is recommended to use potassium magnesium aspartate, potassium citrate, potassium chloride sustained-release tablets[250,251]	Class IIa	Level C

CCB: calcium channel blocker.

can affect the heart, lung, liver, kidney, peripheral circulation, central nervous system and other important systems and organs and affect blood coagulation function,[253] and the morbidity and mortality is high.[254] Studies have shown that age and coexisting chronic congestive HF are important influencing factors for the occurrence of MODSE in elderly hypertensive patients. Hypertensive patients ≥ 70 years old with chronic HF are at high risk of developing MODSE.[255] In recent years, a large-scale clinical study in China included 37,096 elderly patients (694,138 person-time) with an average age of 72.25 years old. In the past ten years, the number of elderly inpatients has been increasing yearly, with an average annual growth rate of 27.48, among which hypertension (36.69%), ischemic heart disease (29.18%) and cerebrovascular disease (13.19%) are the top five major hospitalized diseases, and the proportion of elderly hospitalized comorbidities is as high as 91.36%, of which hypertension combined with ischemic heart disease ranks first.[256] Comorbidities, geriatric syndromes, or MODSE are also risk factors for frailty in elderly patients, the latter having important implications for the effectiveness and adherence to antihypertensive therapy.[256] Therefore, BP management strategies should be fully individualized based on the principle that patients can tolerate antihypertensive therapy, therapy is helpful to maintain, improve vital organ function, and maintain quality of life. When vital organ function deteriorates or acute circulatory dysfunction occurs, active measures should be taken first to maintain stable circulatory function and hemodynamic status, and antihypertensive drugs should be discontinued as appropriate. Patients with MODSE reduce tolerance to antihypertensive drugs, and the risk of drug interactions and adverse reactions is increased, so drug safety should be closely monitored.[257]

There are very few related studies on the management of BP in elderly patients with hypertension combined with MODSE, and individualized treatment can be carried out by referring to the principles of MODSE treatment and the recommendations for BP management in frail patients.[50,258] A multidisciplinary team model is recommended for the management of elderly hypertensive patients with MODSE. Treatment recommendations are shown in Table 27.

SECONDARY HYPERTENSION

Secondary hypertension in elderly individuals is common in clinical practice, accounting for approximately 19.6% of geriatric hypertension cases.[259]

Obstructive Sleep Apnea Hypopnea Syndrome

Obstructive sleep apnea hypopnea syndrome (OSAHS) is characterized by repeated apnea and hypopnea during sleep. In elderly individuals, OSAHS is common and the prevalence rate is as high as 32.5%.[260] Geriatric OSAHS manifests as snoring, daytime sleepiness, sleep apn-

Table 27 Recommendations for the treatment of elderly hypertensive patients with multiple organ insufficiency.

Recommendation	Recommended category	Evidence grading
It is recommended to use tools such as CGA, APACHE II/APACHE III or MODS in elderly patients to comprehensively assess blood pressure status and MODSE and to make treatment decisions, with the goal of promoting the recovery and functional preservation of patients to the greatest extent and reducing the risk of death	Class IIa	Level C
MODSE-inducing factors and underlying diseases should be treated, such as controlling pulmonary infection, improving organ tissue perfusion or circulatory dysfunction, and actively administer nutrition and immune support therapy, etc	Class IIa	Level C
Before initiating antihypertensive therapy, the benefit-risk ratio of antihypertensive therapy should be carefully evaluated, and the impact of blood pressure drops on tissue perfusion and organ function should be closely monitored during treatment; furthermore, hypotension or orthostatic changes in blood pressure should be avoided	Class IIa	Level C
The requirements for blood pressure management can be relaxed in patients with frail status. It is recommended that the reference blood pressure level for starting antihypertensive treatment is systolic blood pressure ≥ 160 mmHg, the reference blood pressure control target is systolic blood pressure < 150 mmHg, and not < 130 mmHg	Class IIa	Level C
Serious complications such as acute stroke, massive hemorrhage and disseminated intravascular coagulation should be actively prevented during antihypertensive treatment	Class IIb	Level C

APACHE: Acute Physiology and Chronic Health Evaluation; CGA: Comprehensive Assessment of Geriatrics; MODS: Multiple Organ Dysfunction Score.

ea, increased nocturia, etc., and is often associated with other systemic complications, such as hypertension, cerebrovascular disease, insulin resistance, and neurological and cognitive impairment.[261]

Polysomnography is the gold standard for diagnosing OSAHS.[262] Wearable devices such as home sleep apnea monitoring can be used as suitable technologies to build a screening system for remote sleep medical systems.[263] The diagnostic criteria of OSAHS in the elderly population are as follows: (1) age ≥ 60 years old; (2) clinical symptoms such as typical nocturnal sleep snoring with apnea, daytime sleepiness [Epworth Sleepiness Scale (ESS) ≥ 9 points] and other symptoms, physical examination showing stenosis and obstruction in any part of the upper airway, apnea-hypopnea index (AHI) ≥ 5 times/h; and (3) for those with insignificant daytime sleepiness (ESS score < 9 points), AHI ≥ 10 times/h or AHI ≥ 5 times/h, there is cognitive impairment, CHD, cerebrovascular disease, DM and insomnia and other comorbidities (1 or more).[264]

Under the premise of improving lifestyles (such as lying on the side, quitting smoking and alcohol, weight loss, etc.), noninvasive positive pressure ventilation and oral appliance therapy are mostly used for the treatment of geriatric OSAHS. Noninvasive positive pressure ventilation is the first choice for patients with moderate to severe OSAHS. Surgical treatment, such as uvulopalatopharyngoplasty, increase the risk of surgery for elderly individuals, and the results are often poor with many complications. Drug treatment with ACEI/ARB antihypertensive drugs is first recommend.

Renal Parenchymal Hypertension

Renal parenchymal hypertension refers to elevated BP caused by renal parenchymal lesions (such as glomerulonephritis), and aging is one of the important risk factors.

The BP target value for elderly patients with CKD aged 60–79 years is < 150/90 mmHg; if tolerated, the BP target can be adjusted to < 140/90 mmHg. The BP target value for elderly individuals over 80 years old is < 150/90 mmHg, but BPs < 130/60 mmHg should be avoided.[264] For most patients with CKD-induced hypertension (including the elderly), the cardiovascular benefits outweigh the risks when the target SBP is < 120 mmHg compared with < 140 mmHg, but there is lack of evidence in the very old patients.[265]

In terms of the selection of antihypertensive drugs, ACEI/ARB drugs are the first choice, especially for patients with proteinuria. Patients with CKD stage 3–4 should be cautious in the use of ACEI/ARB antihypertensive drugs, the initial dose can be reduced by half, and the dynamic changes in serum potassium, serum creatinine and eGFR should be closely monitored to adjust the drugs in time. Since there is no absolute contraindication for the treatment of renal parenchymal hypertension with dihydropyridine CCB, it is especially suitable for patients with abnormal renal function. For CKD patients with excessive volume overload, it is recommended to use diuretics in combination.

Renovascular Hypertension

Renovascular hypertension is hypertension caused by unilateral or bilateral renal artery stenosis for various reasons. The proportion of elderly hypertensive patients with renal artery stenosis is 6.8%,[265] commonly seen in atherosclerosis.

Clues suggesting renal artery stenosis include: (1) persistent hypertension of grade 2 and above, with CHD, peripheral arterial stenosis, etc.; (2) hypertension with mild hypokalemia; (3) hypertension with periumbilical vascular murmur; (4) the BP is suddenly difficult to control under the maintenance of the original antihypertensive drug treatment; (5) refractory or malignant hypertension; (6) renal dysfunction or asymmetrical renal atrophy unable to be explained with other causes; (7) renal dysfunction or asymmetrical renal atrophy unable to be explained with other causes; (8) significant increase in serum creatinine or significant decrease in BP after taking ACEIs or ARBs; and (9) continuous DBP level is > 90 mmHg.

In the clinical screening of renal artery stenosis, renal ultrasound, renal artery computed tomography angiography, and magnetic resonance angiography can be performed. Renal artery angiography is the gold standard for diagnosing renal artery stenosis. It can accurately display the characteristics of the lesion and be used to perform interventional therapy. ACEI/ARB is the first-line treatment of renovascular hypertension and should be used with caution in patients with solitary kidney or bilateral renal artery stenosis. Anti-inflammatory therapy is also required for patients with active Takayasu arteritis. Revascularization of renin-angiotensin system requires different surgical strategies according to different etiologies.[266]

Endocrine Hypertension

Primary aldosteronism

Primary aldosteronism (PA) refers to excessive secreti-

on of aldosterone due to adrenal cortical hyperplasia or tumors, resulting in water and sodium retention, increased blood volume, and inhibiting renin-angiotensin system activity. The clinical manifestations are hypertension with or without hypokalemia.

The main diagnostic tests for PA are the normal saline test and the captopril test, and the screening index is the plasma aldosterone/renin ratio (ARR). Renin declines more significantly than aldosterone in elderly individuals, leading to elevated ARR and false positives.[267] Domestic scholars have proposed that the ARR cutoff value of elderly patients is higher, and ARR 4.4 (ng/dL)/(mU/L) can be used as the primary screening cutoff point for elderly PA, combined with the aldosterone cutoff point 15 ng/dL, which can improve diagnostic specificity; for elderly patients who are not suitable for confirmatory testing, if aldosterone ≥ 23.6 ng/dL and ARR ≥ 4.4 (ng/dL)/(mU/L), the diagnosis of PA can be considered.[268] Adrenal computed tomography examination can clarify the lesions, and bilateral adrenal venous blood sampling is the gold standard for PA function classification.[269]

Treatment of PA depends on the cause and the patient's response to the drug.[270] Surgical treatment (laparoscopic unilateral adrenalectomy) is the first choice for aldosterone adenoma and primary adrenal hyperplasia. For an aldosterone-secreting adrenocortical carcinoma, the primary tumor should be removed as soon as possible. For patients with idiopathic aldosteronism and glucocorticoid-remediable aldosteronism, medication is the first choice.

Pheochromocytoma and paraganglioma

Pheochromocytomas and paragangliomas (PPGLs) mainly synthesize, secrete and release a large amount of catecholamines, causing a series of clinical symptoms, such as elevated BP and metabolic syndromic changes in patients.[271]

The qualitative diagnosis of PPGL is the determination of plasma free or urinary metanephrine and methoxynorepinephrine concentrations (sensitivity: 97%–99%, specificity: 82%–96%). Computed tomographic examination (sensitivity: 85%–98%, specificity: 70%) is the first choice for PPGL tumor imaging for diagnosis and localization. Magnetic resonance imaging can be used as the preferred localization modality or supplementary examination in the following cases (sensitivity: 85%–100%, specificity: 67%): (1) PPGL of skull base or neck; (2) presence of tumor metastasis; (3) retained metal artifacts in the body; (4) allergy to computed tomographic contrast agents; and (5) children, pregnant women, individuals with known germline mutations and people who have recently had excessive radiation and need to reduce their radiation exposure. Iodine-131-meta-iodobenzylguanidine (131I-MIBG) scans are suitable for patients with metastatic or inoperable PPGL, and somatostatin receptor imaging can screen for metastatic paraganglioma lesions. New molecular imaging tests, such as 11C-hydroxyephedrine, ^{18}F-fluorobenzylguanidine, ^{18}F-DOPA and ^{18}F-dihydroxyphenylalanine, are used for clinical screening. PPGL patients need complete genetic screening.[272]

After the diagnosis of PPGL is confirmed, surgical resection should be performed as soon as possible. Except for the parasympathetic paraganglioma of the head and neck and the PPGL that only secretes dopamine, the other patients should be treated with alpha-blockers before surgery. For patients with positive 131I-MIBG radionuclide imaging or inoperable patients, 131I-MIBG radionuclide therapy can be performed. Chemotherapy with cyclophosphamide + vincristine + dacarbazine is the recommended treatment, and the efficacy rate is approximately 50%. Local radiotherapy, gamma knife therapy, radiofrequency ablation and embolization of tumors and metastatic lesions can reduce the clinical symptoms and tumor burden of patients to a certain extent but yield no significant improvements in survival.[272]

Drug-related Hypertension

Drug-related hypertension refers to the 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 cause drug-related hypertension are steroid hormones, nonsteroidal anti-inflammatory drugs, licorice and its active ingredients, erythropoietin, contraceptives, antidepressants, tumor-targeted drugs, etc.[273]

The treatment principles include:[274] (1) immediately stop the drugs that cause hypertension; (2) if the underlying condition requires that the used drugs cannot be stopped or the BP cannot be recovered after withdrawal, the BP should be closely monitored, and corresponding antihypertensive treatment should be given; (3) appropriate BP-lowering regimens should be selected according to specific drugs causing BP elevation and mechanisms affecting antihypertensive effect; and (4) active treatment of complications should be performed.

Tumor-related Hypertension

Elderly patients are a high-risk group for tumors, and hypertension can be one of the symptoms of certain tumor patients. For example, tumors such as pheochromocytoma and cortical adenoma can secrete hormones that cause hypertension; in addition, tumor-induced cachexia and hypercoagulability, as well as renal vascular thromboembolism, can cause hypertension.[275]

For elderly cancer patients, while actively treating the primary disease, clinicians should be alert to hypertension caused by antitumor drugs. Maintaining a healthy lifestyle, reducing psychological stress, and maintaining a positive and optimistic attitude are also the basis for preventing high BP. ACEIs/ARBs, beta-blockers and dihydropyridine CCBs are the first choice for BP.[276]

Interventional Therapy Related to Secondary Hypertension in the Elderly

In recent years, with the continuous development of minimally invasive devices and interventional techniques, renal denervation (RDN), carotid sinus baroreceptor stimulation, central iliac arteriovenous anastomosis, deep cranial nerve stimulation and other interventional treatments have been continuously applied for the treatment of hypertension.

Among these approaches, RDN has certain effectiveness in the treatment of refractory hypertension. According to the experiments named Global Clinical Study of Renal Denervation With the Symplicity Spyral™ Multi-electrode Renal Denervation System in Patients With Uncontrolled Hypertension in the Absence of Antihypertensive Medications (SPYRAL HTN-OFF MED)[277] and Global Clinical Study of Renal Denervation With the Symplicity Spyral™ Multi-electrode Renal Denervation System in Patients With Uncontrolled Hypertension in the Presence of Antihypertensive Medications (SPYRAL HTN ON-MED), the results showed that RDN treatment had a better antihypertensive effect. RDN is a relatively safe interventional therapy with a major adverse event rate of approximately 1.4%. Domestic studies have found that RDN may be safe, effective and feasible in elderly hypertensive patients.

Hypertension-related interventional therapy provides us with a third treatment method for hypertensive patients in addition to lifestyle intervention and drug treatment. Unfortunately, most of the treatment methods lack reliable clinical evidence and need to be further explored in the future.

Recommendations for the management of secondary hypertension in the elderly population are shown in Table 28.

COMMUNITY SUPPORT AND REMOTE MANAGEMENT

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, are prone to orthostatic hypotension, postprandial hypotension, abnormal BP circadian rhythms, white coat hypertension, etc., and often have multiple diseases simultaneously and take multiple drugs 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 staff have a

Table 28 Recommendations for the management of secondary hypertension in the elderly population.

Recommendation	Recommended category	Evidence grading
Polysomnography is recommended for screening elderly patients with OSAHS	Class I	Level A
Noninvasive positive pressure ventilation is recommended for patients with moderate to severe OSAHS	Class I	Level A
It is recommended to improve renal arteriography in elderly patients with renovascular hypertension	Class I	Level A
Bilateral adrenal venous blood sampling is recommended for functional typing of elderly patients with primary aldosteronism	Class I	Level B
Genetic testing is recommended for patients with pheochromocytoma and paraganglioma	Class IIa	Level C
Renal sympathetic denervation may be considered for elderly patients with secondary and refractory hypertension	Class IIa	Level C

OSAHS: obstructive sleep apnea hypopnea syndrome.

better understanding of residents' health status and living habits, so interventional measures are more targeted. Guidance by relatively familiar and trusted community workers can improve compliance in elderly hypertensive patients. In addition to medical services, the community can also provide meticulous family and humanistic care.

Follow-up support

Elderly hypertensive patients need systematic and long-term follow-up and management, which needs to be done by the community. Community follow-up can be done in a variety of ways, such as household follow-up, home monitoring, wearable device monitoring, and remote services.

Health education

Most hypertensive patients seek treatment in primary medical institutions, primary medical or health management institutions and primary medical staff, including community health service centers (stations), township health centers, village health centers, health care centers, and health education institutes, which are a major force in BP education. Guidance and education should be carried out in a targeted manner based on the characteristics of elderly individuals.

Environmental support

A favorable community environment should be created, elderly hypertensive patients should be encouraged to adopt a healthy lifestyle, and elderly people with better mobility should be encouraged to visit community health service centers for regular follow-up visits and should receive health education to prevent the occurrence of MI, stroke and other cardiovascular and cerebrovascular diseases. Patients should receive immediate medical attention in the event of an accident.

Humanistic care

Due to rapid changes in social roles, elderly individuals are prone to adverse psychological changes and problems such as functional decline, limited activities, and emotional loneliness. Without appropriate care, hypertension management cannot achieve the desired effect. According to the characteristics of elderly individuals, psychological counseling can be carried out. For empty nesters, representatives from neighborhood committees and medical institutions should conduct regular visits to provide emotional support and home medical services.

Remote Management

Advantages of hypertension remote management

Remote dynamic monitoring helps the attending physician grasp the fluctuation of BPs of the patient in real time, predict changes in the condition, take timely treatment measures, to prevent deterioration of the disease, and implement the individualized treatment plan. At the same time, through the use of remote video and other technologies, high-quality expert resources can be utilized for training, consultation and guidance to improve the level of diagnosis and treatment.

Contents of hypertension remote management

Remote management mainly includes monitoring data and assessing risk in a timely manner, optimizing treatment, conducting lifestyle interventions, enriching the content of health education, and dealing with emotional problems of elderly individuals. In recent years, online consultations, examination appointments, and drug delivery have also been carried out, which greatly facilitates elderly individuals in seeking medical treatment.[126]

Based on the above functions, the 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.[278] By integrating the timeliness, accessibility, and individuality of internet technology with the particularity of the elderly hypertensive group, the optimal management can be achieved.

"Three Highs" Comanagement

The "three highs", namely, hypertension, DM, and dyslipidemia, are the most important risk factors for CVD, as well as the most controllable and reversible metabolic risk factors. The prevention and treatment of CVD in the elderly population in China should also focus on the main risk factors for CVD. At present, the current situation of hypertension, DM and dyslipidemia in China is not optimistic, and the comprehensive management status is not good.[279] Up to 30% of the population suffer from hypertension, DM and dyslipidemia simultaneously.[280] However, only 14% of diabetic patients meet the standards of BP and blood sugar control at the same time, and less than 20% of them reach the standards for blood sugar and blood lipids.[281]

The "three highs" comanagement is a systematic project that requires not only the support of government health policies, social health environment, and citizens' health behaviors but also the support of evidence-based medical evidence such as major research results and clinical skills and experience. More importantly, it is necessary to improve compliance, improve clinical inertia, and establish a health care mechanism.

Specifically, this approach focuses on management from the following four aspects. Firstly, build a comanagement system. Improve the comprehensive prevention and treatment mechanism of chronic diseases under the leadership of the government, the cooperation of departments, and the participation of the whole population. Integrate health into all policies, mobilize the enthusiasm of society and individuals to participate in prevention and treatment, and build a "three highs" comanagement system in which medical institutions at all levels are linked together. Secondly, conduct early screening assessments. The full implementation of the first-diagnosis BP measurement for people over 18 years old should be advocated, and community health service centers and township health centers gradually improve the frequency of fasting blood glucose and blood lipid examinations for people aged ≥ 40 years once a year. CVD risk stratification should be performed according to the "three highs" levels, other risk factors, target organ damage, and concomitant clinical diseases; moreover, BP, blood lipids, and blood glucose management targets should be individually selected. Thirdly, integrate disease management. Equal attention should be given to the management of hypertension, DM, and dyslipidemia. The comprehensive control objectives of risk factor management in different populations should be precise, and standardized lifestyle changes and drug treatment interventions should be carried out to improve the efficiency of interventions. Follow-up management is also particularly important. Last but not least, advocate self-health management. CVD is a disease closely related to life behaviors. Individual health behaviors and health concepts are crucial to the prevention and control of diseases and permeate the prevention and treatment of diseases. Enhance the patients' self-health awareness, continuously improve patients' health management ability, standardize patients' personal health behaviors, improve patients' treatment compliance, so that they can actively obtain health knowledge and cooperate with the treatment measures of professional institutions.

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Guideline Writing and Review Committee

Co-Chairs: Li FAN (Chinese PLA General Hospital), Qi HUA (Xuanwu Hospital, Capital Medical University)

Vice Chairs: Lu-Yuan CHEN (Guangdong Provincial People's Hospital), Yi-Fang GUO (Hebei General Hospital), Jing LI (Xuanwu Hospital, Capital Medical University), Lin PI (Chuiyangliu Hospital Affiliated Tsinghua University), Zeng-Wu WANG (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Liang-Di XIE (The First Affiliated Hospital of Fujian Medical University), Hong YUAN (The Third Xiangya Hospital of Central South University), Xin-Jun ZHANG (West China Hospital, Sichuan University)

Guideline Writing Committee Members

Feng CAO (Chinese PLA General Hospital), Lu-Yuan CHEN (Guangdong Provincial People's Hospital), Wei-Wei CHEN (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Li FAN (Chinese PLA General Hospital), Yi-Fang GUO (Hebei General Hospital), Yi-Xin HU (Chinese PLA General Hospital), Qi HUA (Xuanwu Hospital, Capital Medical University), Yi-Nong JIANG (The First Affiliated Hospital of Dalian Medical University), Jing LI (Xuanwu Hospital, Capital Medical University), Wei-Ming LI (The First Affiliated Hospital of Harbin Medical University), Yan LI (Ruijin Hospital, Shanghai Jiaotong University School of Medicine), Yong LI (Huashan Hospital, Fudan University), Yue LI (The First Affiliated Hospital of Harbin Medical University), Qing-Feng MA (Xuanwu Hospital, Capital Medical University), Lin PI (Chuiyangliu Hospital Affiliated Tsinghua University), Ying SHAN (Huashan Hospital, Fudan University), Xi-Peng SUN (Xuanwu Hospital, Capital Medical University), Jing TAN (Xuanwu Hospital, Capital Medical University), Zeng-Wu WANG (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Hai-Ying WU (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Wei YANG (Xu-

anwu Hospital, Capital Medical University), Xin-Jun ZHANG (West China Hospital, Sichuan University), Jiu-Chang ZHONG (Beijing Chao-Yang Hospital, Capital Medical University)

Guideline Review Committee Members (sorted by last name character in Chinese)

Pei-Li BU (Qilu Hospital of Shandong University), Feng CAO (Chinese PLA General Hospital), Jian CAO (Chinese PLA General Hospital), Lu-Yuan CHEN (Guangdong Provincial People's Hospital), Qi-Ling CHEN (Peking University People's Hospital), Wei-Wei CHEN (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Xiao-Ping CHEN (West China Hospital, Sichuan University), Yuan-Yuan CHEN (Peking University People's Hospital), Hong-Liang CONG (Tianjin Chest Hospital), Ai-Ming DANG (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Li FAN (Chinese PLA General Hospital), Zhen-Xing FAN (Xuanwu Hospital, Capital Medical University), Ying-Qing FENG (Guangdong Provincial People's Hospital), Jing GAO (Xuanwu Hospital, Capital Medical University), Ping-Jin GAO (Ruijin Hospital, Shanghai Jiaotong University School of Medicine), Jin-Cheng GUO (Beijing Luhe Hospital, Capital Medical University), Yi-Fang GUO (Hebei General Hospital), Qing HE (Beijing Hospital), Yi-Xin HU (Chinese PLA General Hospital), Qi HUA (Xuanwu Hospital, Capital Medical University), Yi-Nong JIANG (The First Affiliated Hospital of Dalian Medical University), Dong-Bao LI (Beijing Friendship Hospital, Capital Medical University), Jing LI (Beijing Hospital), Jing LI (Xuanwu Hospital, Capital Medical University), Nan-Fang LI (Xinjiang Uiger Municipal People's Hospital), Wei-Ming LI (The First Affiliated Hospital of Harbin Medical University), Yan LI (Ruijing Hospital, Shanghai Jiaotong University School of Medicine), Yan-Fang LI (Beijing Anzhen Hospital, Capital Medical University), Yong LI (Huashan Hospital, Fudan University), Yue LI (The First Affiliated Hospital of Harbin Medical University), Dong-Xia LIU (Hebei General Hospital), Jing LIU (Peking University People's Hospital), Mei-Lin LIU (Peking University First Hospital), Min LIU (Henan Provincial People's Hospital), Wei LIU (Beijing Hospital), Zhi LIU (Xuanwu Hospital, Capital Medical University), Xin-Zheng LU (Jiangsu Provincial Hospital), Qing-Feng MA (Xuanwu Hospital, Capital Medical University), Zhi-Yi MA (Beijing Tsinghua Changgung Hospital), Jian-Jun MOU (The First Affiliated Hospital of Xi'an Jiaotong University), Lin PI (Chuiyangliu Hospital Affiliated Tsinghua University), Ying SHAN (Huashan Hospital, Fudan University), Qian-Hui SHANG (Affiliated Hospital of Zunyi Medical University), Yan SHU (Sichuan Provincial People's Hospital), Qiang SU (Jiangbin Hospital of Guangxi Zhuang Autonomous Region), Ning-Ling SUN (Peking University People's Hospital), Xi-Peng SUN (Xuanwu Hospital, Capital Medical University), Jing TAN (Xuanwu Hospital, Capital Medical University), De-Zhao WANG (Beijing United Family Hospital), Hong-Yi WANG (Peking University People's Hospital), Ji-Guang WANG (Ruijin Hospital, Shanghai Jiaotong University School of Medicine), Jie-Yu WANG (Xuanwu Hospital, Capital Medical University), Qing WANG (Fuxing Hospital, Capital Medical University), Sheng-Huang WANG (The First Affiliated Hospital of Ningbo University), Yan-Ling WANG (Xuanwu Hospital, Capital Medical University), Zeng-Wu WANG (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Hai-Ying WU (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Qiang WU (The Sixth Medical Center, Chinese PLA General Hospital), Zhong WU (Hainan General Hospital), Yang XI (Peking University People's Hospital), Liang-Di XIE (The First Affiliated Hospital of Fujian Medical University), Li-Qing XU (Shenzhen New Frontier United Family Hospital), Wei YANG (Xuanwu Hospital, Capital Medical University), Xiao-Ming YANG (Sir Run Run Shaw Hospital, Zhejiang University School of Medicine), Jing YU (The Second Hospital & Clinical Medical School, Lanzhou University), Hong YUAN (The Third Xiangya Hospital of Central South University), Li ZHANG (Chinese PLA General Hospital), Xin-Jun ZHANG (West China Hospital, Sichuan University), Yu-Qing ZHANG (Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), De-Chao ZHAO (The First Affiliated Hospital of Harbin Medical University), Luo-Sha ZHAO (The First Affiliated Hospital of Zhengzhou University), Jiu-Chang ZHONG (Beijing Chao-Yang Hospital, Capital Medical University), Ping ZHONG (Sichuan Provincial People's Hospital), Zhi-Ming ZHU (Army Medical Center of Chinese PLA)

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