Chinese Medical Journal®

Clinical practice guidelines for the management of hypertension in China

Chinese Society of Cardiology, Chinese Medical Association; Hypertension Committee of Cross-Straits Medicine Exchange Association; Cardiovascular Disease Prevention and Rehabilitation Committee, Chinese Association of Rehabilitation Medicine

Abstract

In China, hypertension is the most common chronic non-communicable disease and the most significant risk factor for cardiovascular mortality among urban and rural residents. To standardize the clinical diagnosis and treatment of hypertension and to improve the prevention and control level of hypertension in China, Chinese Society of Cardiology, Chinese Medical Association; Hypertension Committee of Cross-Straits Medicine Exchange Association; Cardiovascular Disease Prevention and Rehabilitation Committee, Chinese Association of Rehabilitation Medicine, jointly collaborated to formulate the Clinical Practice Guideline for Hypertension Management in China. The Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) approach was used to rate the quality of evidence and strength of recommendations, and the reporting items for practice guidelines in healthcare (RIGHT) were followed to establish the guidelines. Detailed evidence-based recommendations for the diagnosis, evaluation, and treatment of 44 clinical questions in the field of hypertension, including essential and secondary hypertension, have been provided to guide clinical practice.

Registration: International Practice Guidelines Registry Platform, http://www.guidelines-registry.cn/, No. IPGRP-2021CN346.

Keywords: China; GRADE; Guidelines; Hypertension; Management

Introduction

In China, hypertension is one of the most common chronic diseases and also the most important risk factor for cardiovascular disease (CVD) death among urban and rural residents, seriously affecting the health and economic and social development of individuals. Overall, 23.2% (around 244.5 million) of the Chinese adult population ≥18 years has hypertension, based on the definition of a systolic blood pressure (SBP) ≥140 mmHg or a diastolic blood pressure (DBP) ≥90 mmHg.[1] However, the awareness, treatment, and control rates of hypertension in China are still low at 51.6%, 45.8%, and 16.8%, respectively.[2] Recently, with the increasing evidence of hypertension and related diseases, many countries and regions have revised or updated their hypertension guidelines.[3–6] However, accumulating evidence from hypertension-related studies and clinical trials in the Chinese population suggests the need for revision of hypertension guidelines in China. Therefore, it is necessary to define the quality of evidence and strength of recommendations based on the best available evidence to address key clinical issues such as hypertension screening, diagnosis, assessment, and treatment, considering health economics, to develop the Chinese Clinical Practice Guidelines for Hypertension as guidelines for clinical practice.

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000003431

Method for Developing the Guideline

The guideline was registered in the International Practice Guideline Registry Platform in English and Chinese (registration No. IPGRP-2021CN346). The protocol for the guidelines has been published previously.[7] The process and details of the guideline formulation principles, development institutions, target users, applicable population, determination of clinical questions and outcomes, evidence synthesis and assessment, patient preference and values survey, development of recommendations, peer review of the guidelines, and publication and updating of the guidelines are detailed in the protocol.

In the actual formulation of the guidelines, considering many factors, the following contents of the protocol were adjusted and improved: First, the number of members in the guideline working group was adjusted. The guideline working group comprised four groups: (1) Guideline Advisory Committee, which comprised eight senior clinicians specializing in CVDs; (2) Guideline Development Group, which comprised 61 panelists from various disciplines, including cardiologists, nephrologists,

Correspondence to: Jun Cai, Beijing Anzhen Hospital, Capital Medical University, No. 2 Anzhen Road, Chaoyang District, Beijing 100029, China; Chinese Institutes for Medical Research, No. 10, xitoutiao, youan men, Fengtai District, Beijing 100069, China
E-Mail: caijun7879@126.com;
Ying Lou, Department of Cardiology, Fuwai Hospital Chinese Academy of Medical Sciences, No. 167 Beilishi Road, Xicheng District, Beijing 100037, China
E-Mail: fuwailou1798@sina.com

Chinese Medical Journal 2024;XX(XX)

Received: 15-10-2024; **Online:** 09-12-2024 **Edited by:** Rongman Jia

endocrinologists, urological surgeon, vascular surgeon, psychiatrist, epidemiologist, nurse, clinical pharmacist, health economist physician, and patients; (3) Evidence Review Group, which comprised 51 panelists, including 34 clinicians, 15 evidence-based medical experts, and 2 coordinators; and (4) External Review Group, which comprised of three hypertension physicians who were not directly involved establishing these guidelines. The composition and responsibilities of each group are listed in the guideline protocol.[7] Second, we clarified the management policies and procedures for conflicts of interest (COI). The Guideline Working Group required all panelists to complete a COI declaration form. The collected COI declaration forms were evaluated and managed by the Guideline Advisory Committee under the supervision of the methodology Chair. If the panelists of the Guideline Working Group had a declared interest that was defined as COI, then depending on the extent of the conflict, panelists in the core work would be restricted or excluded from the development of these guidelines. All COI declaration forms were made available by contacting the Guideline Working Group. Third, the funding sources were adjusted. The development of these guidelines was supported by the Project of the Bureau for Disease Control and Prevention, National Health Commission (Project ID: T2021-ZC02). These funds are mainly used to cover labor, materials, travel, and conference expenses. Finally, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to assess and rate the quality of evidence and strength of the recommendations [Table 1].[8] For some clinical questions that were not supported by evidence, recommendations were developed through expert consensus, which is called a good practice statement (GPS).[9] After a comprehensive consideration of the preferences and values of Chinese patients, costs, benefits, harms of interventions, and other factors, preliminary draft recommendations were developed. On June 4, 2022, the first round of the Delphi recommendation survey was conducted among experts of the Guideline Development Group, and nine recommendations did not reach a consensus (consensus degree <75%). For recommendations that did not reach a consensus, online expert consensus meetings were held on June 18 and 19, 2022. The second round of the Delphi recommendation survey was conducted on June 23, 2022, based on the revised recommendations from expert opinions. Finally, a consensus was reached on all clinical questions (consensus degree ≥75%). In the process of establishing the guideline, if new evidence emerged, the contents of some clinical problems will be adjusted and modified.

Clinical Question 1: What are the Rational Diagnostic Criteria for Hypertension in Chinese Adults?

Recommendations

An SBP of ≥140 mmHg and/or a DBP of ≥90 mmHg is recommended to define hypertension (1B).

An SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg is recommended as prehypertension (1B).

Evidence and rationale

In the World Health Organization's Global Report on Hypertension in 2023, based on extensive observational studies conducted worldwide, experts highlighted that when the SBP is ≥115 mmHg, the risk of CVD steadily increases with elevated SBP levels.[10–19] According to recent studies in China, approximately 2.67 million cardiovascular deaths in 2018 were attributable to SBP levels ≥115 mmHg, leading to a loss of approximately 48.16 million life-years, clearly indicating an upward trend.[20] However, the development of rational diagnostic criteria for hypertension also needs to consider the efficacy and safety of anti-hypertensive interventions for various blood pressure (BP) levels, cost-effectiveness of anti-hypertensive interventions, availability of healthcare resources, and various aspects of social impact.

To date, various randomized controlled clinical trials (RCTs) and meta-analyses, both domestic and international, have provided evidence of the efficacy and safety

Table 1: Grading of quality of evidence and strength of recommendations for clinical practice guidelines for the management of hypertension in China.

GRADE	Description
Quality of evidence	
High quality of evidence (A)	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality of evidence (B)	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality of evidence (C)	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low quality of evidence (D)	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.
Strength of recommendation	
Strong (1)	The advantages of intervention significantly outweigh the disadvantages or the disadvantages of intervention significantly outweigh the advantages.
Weak (2)	The advantages of intervention may outweigh the disadvantages or the disadvantages of intervention may outweigh the advantages or the relationship between advantages and disadvantages is not clear.

GRADE: Grading of recommendations, assessment, development, and evaluation.

of anti-hypertensive drug therapy for individuals with an SBP ≥140 mmHg and/or a DBP ≥90 mmHg.[21–27] Health economics evaluation studies have also shown that anti-hypertensive treatments are cost-effective for individuals with the aforementioned BP levels.[28] In China, an SBP ≥140 mmHg and/or a DBP ≥90 mmHg has been used as a diagnostic criterion for hypertension since 1999 and has been widely promoted in clinical practice. Currently, this criterion is also recommended in the hypertension-related guidelines issued by the World Health Organization and most national or regional professional associations.[3,19,29,30] Therefore, based on the comprehensive evaluation of existing clinical research evidence both domestically and internationally, the results of health economic assessments, the demand for healthcare resources for hypertension prevention and treatment, and the influence of various social factors, this guideline recommends that the diagnostic criteria for adult hypertension should be maintained at an SBP of ≥140 mmHg and/or a DBP of ≥90 mmHg.

Meanwhile, based on the relationship between BP levels and the risk of CVD, as well as the national strategy to advance CVD prevention and treatment,[31] this guideline suggests the importance of further approaches to preventing and treating hypertension in individuals with an SBP level of 130–139 mmHg and/or a DBP level of 80–89 mmHg, who are mainly young and middle-aged people (aged 18–54 years).[1] Numerous domestic and international studies have reported that 65–70% of individuals with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg had hypertension within 10–15 years.[10,32] This BP stratum can lead to a significantly increased risk of CVD if accompanied by cardiovascular, cerebrovascular, and renal comorbidities; target organ damage; diabetes mellitus; or multiple cardiovascular risk factors.[32] Several meta-analyses of RCTs have provided preliminary evidence for the efficacy and safety of anti-hypertensive drug therapy in the primary and secondary prevention of hypertension in individuals with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg.[21,22,27,33] Health economics evaluation studies have also confirmed the cost-effectiveness of using anti-hypertensive medications in this population.[34] Therefore, this guideline recommends an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg as prehypertension.

Both hypertensive and prehypertensive individuals require CVD risk evaluation and risk stratification based on age, the presence of cardiovascular, cerebrovascular and renal comorbidities, target organ damage, diabetes mellitus, and other cardiovascular risk factors to provide evidence for clinical treatment decisions.

Clinical Question 2: How to Simplify Cardiovascular Risk Stratification among Patients with Hypertension or Prehypertension?

Recommendations

Hypertensive and prehypertensive patients can be stratified as patients at a high risk of CVD or those without a high risk of CVD.

The following individuals are considered at high risk for CVD: (1) Individuals with an SBP ≥140 mmHg and/or a DBP ≥90 mmHg; (2) Individuals with an SBP 130–139 mmHg and/or a DBP 80–89 mmHg, and with existing CVD, or concomitant hypertension-mediated organ damage (HMOD), or accompanied with ≥3 cardiovascular risk factors.

Those with an SBP 130–139 mmHg and/or a DBP 80–89 mmHg and the absence of the above high-risk conditions are considered as non-high CVD risk.

Evidence and rationale

Guidance is needed to select patients who are most likely to benefit from BP-lowering treatments. Thus, implementing a risk-based approach to guide the timing of pharmacological treatment initiation in patients with hypertension is necessary. For clinicians, simpler risk assessments are easier to understand and implement. In previous guidelines, the risk of CVD is considered low (<5%), intermediate (5–9%), and high (≥10%) according to the calculated 10-year CVD risk.[32] Recently, more studies have shown that >80% of patients with an SBP of ≥140 mmHg and/or a DBP of ≥90 mmHg have more than two risk factors.[35,36] Thus, intermediate-risk patients defined by previous guidelines can be considered to be at a high risk of CVD.[32] Previous CVD risk assessments are no longer suitable for current clinical practice. Therefore, the risk assessment among patients with hypertension or prehypertension in this guideline is simplified as high-risk or non-high-risk of CVD.

Summary of the CVD risk stratification approach

(1) Patients with an SBP of ≥140 mmHg and/or a DBP of ≥90 mmHg are directly stratified as high-risk patients.

(2) For patients with an SBP 130–139 mmHg and/or a DBP 80–89 mmHg, and with established CVD who are at increased risk of recurrent CVD outcomes or death, anti-hypertensive treatment was associated with a risk reduction of major adverse cardiovascular events (MACEs) and death.[32] These individuals were stratified as having a high CVD risk.

(3) For patients with an SBP 130–139 mmHg and/or a DBP 80–89 mmHg, and with HMOD, well-controlled BP is beneficial for delaying the progression of end-organ damage; these patients are also stratified as having a high risk of CVD.

(4) By referring to the recommendations of the 2020 Chinese Guidelines for Primary Prevention of Cardiovascular Disease[32] and based on the prospective epidemiological data of the Chinese population, it was estimated that the 10-year risk of atherosclerotic CVD (ASCVD) was basically ≥10% in patients with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg with ≥3 cardiovascular risk factors. The 10-year risk of ASCVD was basically ≥10%, which was considered high risk. Those with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg who did not meet the above definition of high-risk patients were

classified as non-high-risk patients. A summary of cardiovascular risk factors, HMOD, and established clinical CVDs is presented in Table 2.[37–42]

Clinical Question 3: How do you Choose BP Measurement Methods and Devices?

Recommendations

BP measurement devices: We suggest adults use upper-arm electronic sphygmomanometers that have been validated with a standardized protocol (1B).

BP measurement methods: (1) Have the patient relaxed, sitting in a chair (feet on the floor, back supported, and legs uncrossed) for 3–5 min. Rest the patient's arm on a desk and position the middle of the cuff at the level of the heart (1D). (2) Use the correct cuff size (such that the bladder encircles 75–100% of the individual's arm and the width encircles 37–50%; a bladder with 12 cm in width and 22–26 cm in length should meet the needs of most adults). Wrist-cuff electronic sphygmomanometer may be considered in those with arm circumference >42 cm (1B). (3) Remove all clothing covering the arm, leaving only a thin layer if necessary (avoid rolling up the sleeve). The lower end of the cuff should be 2–3 cm above the antecubital fossa (1C). (4) Separate repeated measurements by 1–2 min should be performed, and the average should be taken; if the two readings differ by >10 mmHg, a third measurement is needed, and the average of the last two readings should be taken. At the initial visit, the BP should be measured in both arms, and the higher BP value should be used (2C). (5) Electronic sphygmomanometers are suggested in patients with atrial fibrillation (AF), with at least three BP measurements required, with the average of the three readings taken (1C).

Table 2: Factors affecting risk stratification among hypertensive or prehypertensive patients.

Cardiovascular risk factors
Age (male ≥45 years old, female ≥55 years old)
Smoking or passive smoking
HDL-cholesterol <1.04 mmol/L (40 mg/dL)
LDL-cholesterol ≥3.40 mmol/L (130 mg/dL)
Abnormal fasting blood glucose (6.1–6.9 mmol/L)
Obesity (BMI ≥28.0 kg/m^2)
HMOD
Left ventricular hypertrophy (electrocardiography and echocardiography) or left atrium enlargement (echocardiography)
Carotid plaque
baPWV ≥18 m/s or cfPWV ≥10 m/s
ABI ≤0.9
Established clinical comorbidities
Cerebral hemorrhage/cerebral infarction, transient ischemic attacks, CHD, chronic HF, AF
LDL-cholesterol ≥4.9 mmol/L (190 mg/dL) or total cholesterol ≥7.2 mmol/L (278 mg/dL)
CKD, eGFR <60 mL·min^{-1}·1.73 m^{-2}, or albuminuria ≥30 mg/24 h, or ACR ≥30 mg/g
Diabetes mellitus
Aortic disease or peripheral artery disease
Hypertensive retinopathy (fundus hemorrhage or exudation, papilledema)

ABI: Ankle-brachial index; ACR: Albumin-to-creatinine ratio; AF: Atrial fibrillation; BMI: Body mass index; baPWV: Brachial-ankle pulse wave velocity; cfPWV: Cervical-femoral pulse wave velocity; CHD: Coronary heart disease; CKD: Chronic kidney disease; eGFR: Estimated glomerular filtration rate; HF: Heart failure. HDL: High-density lipoprotein; HMOD: Hypertension-mediated organ damage; LDL: Low-density lipoprotein.

Evidence and rationale

Accurate BP measurement is the basis for screening, diagnosing, and managing hypertension, and using a valid BP measurement device and a suitable method are of vital importance. Mercury sphygmomanometers have gradually been replaced by electronic sphygmomanometers because of mercury pollution.[43] Compared with mercury sphygmomanometers, the accuracy of upper-arm electronic sphygmomanometers has been successfully validated by the American Association for the Advancement of Medical Instrumentation, European Society of Hypertension, and International Organization for Standardization (AAMI/ESH/ISO), which was developed in 2018.[44,45] Therefore, the use of upper-arm electronic sphygmomanometers for BP measurements is recommended.

Most domestic and international guidelines recommend that 30 min before BP measurement, strenuous exercise should be avoided, smoking should be avoided, alcohol and coffee should not be consumed, and the bladder should be empty.[46,47] Results of a systematic review also showed that the accuracy of BP values was affected by exercise, smoking, drinking, caffeine intake, and bladder filling before measurement.[48]

Regarding the duration of rest, few studies have directly compared rest for 3–5 min *vs.* 5 min before BP measurement; however, the result from an RCT showed that the BP difference was within ±2 mmHg between rest for 2 min and 5 min.[49] To improve the compliance of patients and the efficiency of BP measurement, this guideline suggests taking a rest of 3–5 min before BP measurement. During measurement, rest the patient's upper arm on a table and position the middle of the cuff at the heart level.[30,50] BP measurement results can be affected by the length and width of the cuff. Current guidelines suggest selecting an appropriate cuff according to the arm circumference.[30,50] The cuff, which is 12 cm wide and 22–26 cm long, can fit the range of arm sizes in most adults. However, for obese patients with hypertension with arm circumference >42 cm, results from a systematic review showed that compared with the reference of a correctly fitting upper arm cuff, BP measurement at the wrist had a sensitivity of 0.92 (95% confidence interval [CI]: 0.64–0.99) and a specificity of 0.92 (95% CI: 0.85–0.87), which were superior to those of an incorrectly fitting upper arm cuff (sensitivity of 0.73, 95% CI: 0.67–0.78; specificity of 0.76, 95% CI: 0.69–0.82).[51] Results from a systematic review showed that measuring BP over a thick sleeve or below a rolled-up sleeve may result in an overestimation

of BP. However, there is no significant difference between measuring BP on a thin sleeve and on a bare arm (mean difference [MD] = 0.59 mmHg, 95% CI: −0.11 mmHg to 1.30 mmHg).[52]

Regarding the number of measurements during a visit, some guidelines recommend that if the difference in BP between the first two measurements exceeds 10 mmHg, a third measurement should be performed.[29] Studies have shown that taking an average of three measurement readings resulted in a slightly higher BP value than taking the last two readings; however, the difference was negligible. The prevalence rates of hypertension diagnosed using these two methods were 33.6% and 33.5%, respectively.[53] For convenience in clinical practice, this guideline suggests taking the average of the last two measurement readings as the BP level. Approximately 80% of patients with AF have hypertension.[54] The variations in myocardial contractility and ventricular filling cause stroke volume variation in patients with AF, and all of the above factors increase beat-to-beat BP variability. Currently, neither AF nor hypertension guidelines provide clear recommendations for BP measurements and calibration methods. Studies have found that calculating the average of three BP readings measured using an upper-arm electronic sphygmomanometer can reduce the margin of error caused by arrhythmia in patients with AF.[55]

Clinical Question 4: For Diagnosis and Management of Hypertension, is it based on Office BP Measurement (OBPM), Home BP Monitoring (HBPM), or 24-h Ambulatory BP Monitoring (ABPM)?

Recommendations

Hypertension can be diagnosed based on OBPM, ABPM, or HBPM, with ABPM preferred if available (2C).

HBPM is recommended as the first choice for hypertension management. If this is not possible, combining OBPM with ABPM for management is recommended (2C).

Evidence and rationale

Hypertension cannot be diagnosed based on BP measurements from a single visit. Studies have shown that the sensitivity of OBPM in the diagnosis of hypertension is only 51% (95% CI: 36–67%), with a specificity of 88% (95% CI: 80–96%),[56] and that OBPM is prone to the white coat effect. Although the sensitivity of HBPM is 75% (95% CI: 65–86%) and is higher than that of OBPM, its specificity is only 76% (95% CI: 65–86%).[56] ABPM can provide an average BP value for 24 h and assess the variability of BP within 24 h with high stability and repeatability.[57] It can identify white-coat and masked hypertension, leading to a more accurate diagnosis. Chinese studies have also shown that ABPM is superior to HBPM in the diagnosis of white-coat, masked, and sustained hypertension.[58] However, owing to the poor accessibility of ABPM in some areas of China, OBPM and HBPM remain the main methods for BP monitoring. Therefore, the guideline recommends that the diagnosis of hypertension should be based on OBPM, ABPM, and HBPM, with ABPM as the preferred option when available. OBPM and HBPM measurements should be standardized, and unstandardized BP values should not be used as a basis for the diagnosis and treatment of hypertension.

According to the outcomes such as cardiovascular events and death, as well as the 10-year CVD risk prediction performance, OBPM ≥140/90 mmHg corresponded to the daytime mean and mean 24-h ABPM thresholds of ≥135/85 mmHg and ≥130/80 mmHg,[59] respectively. The corresponding diagnostic threshold for HBPM is ≥135/85 mmHg.[60]

Out-of-office BP monitoring, including HBPM and ABPM, has good predictive power for cardiovascular events and mortality outcomes.[61,62] However, ABPM is not easy to obtain in daily life, and long-term 24 h ABPM will affect the normal life of patients, especially night sleep[63]; thus, ABPM is not recommended as the first choice for hypertension management. Studies have shown that HBPM is associated with reductions in office SBP (MD: −3.12 mmHg, 95% CI: −4.78 mmHg to −1.46 mmHg) and DBP (MD: −1.44 mmHg, 95% CI: −2.13 mmHg to −0.74 mmHg) over 12 months of follow-up compared with usual care and improves patient medication adherence,[64,65] suggesting that HBPM-based BP management is preferred. When HBPM cannot be performed, BP should be managed based on multiple OBPM over different days, in conjunction with ABPM whenever possible.

Clinical Question 5: How to Recommend the Timing and Frequency of Measurements for Home BP Monitoring in Hypertensive Patients?

Recommendations

BP measurements should be taken both in the morning and evening. Obtain at least two consecutive BP readings each session, with a 1-min to 2-min interval between them. Calculate the average of these two readings; if the difference is greater than 10 mmHg, take a third reading and average the last two. Before measuring BP, refrain from exercise, alcohol, caffeine, and smoking for at least 30 min, and rest quietly for 3–5 min (1D).

It is advised to measure BP before medication intake or breakfast and after emptying the bladder (1B).

Evening BP measurements should ideally be taken before dinner; if not feasible, it is suggested to measure within an hour before bedtime (2D).

For those newly diagnosed with hypertension or whose BP is uncontrolled, HBPM on at least three consecutive days weekly is recommended (1B).

For individuals with well-regulated BP, HBPM can be performed once or twice a week (2D).

Evidence and rationale

HBPM offers several advantages over traditional OBPM in a clinical setting, including (1) the ability to identify conditions such as white-coat, masked, morning, and resistant hypertension; (2) it is a superior method for tracking patient responses to anti-hypertensive therapy; and (3) it is more closely associated with the risk of hypertension-induced end-organ damage and cardiovascular events.[50,56–66]

To facilitate the diagnosis of hypertension using HBPM, patients should record their BP for a minimum of three consecutive days before a clinic visit. BP should be measured in the morning and evening, with at least two readings taken at 1–2 min intervals. This protocol is equally applicable to patients with hypertension and suboptimal BP control. These recommendations are supported by studies indicating that the hazard ratio (HR) for predicting cardiovascular events in patients whose BP was measured twice daily for three consecutive days was 1.039 (95% CI: 1.006–1.074), with an HR of 1.057 (95% CI: 1.012–1.104) for 7 days of HBPM. The difference in HR between 3 days and 7 days of monitoring was negligible and minimally added to the prognostic value. Thus, a 3-day HBPM regimen was considered adequate for reliably predicting cardiovascular risk.[67] A systematic review conducted in 2019 also indicated that increasing the number of BP measurement days may enhance predictive capabilities. Three-day measurements increased the predictive accuracy from 72% to 91% of the maximum theoretical value, whereas seven-day measurements increased this to 96%. However, measuring after 3 days did not show a strong correlation with ABPM.[68] For patients with well-controlled BP, HBPM for 1–2 days/week aligns with the most current guidelines.[30]

A systematic review from 2017 analyzed the factors affecting BP measurements. Among the 29 potential factors, eight were related to patients, including meal intake immediately before measurements, alcohol and coffee consumption, smoking, a full bladder, and insufficient rest time. These factors may skew the estimation of actual resting BP.[48] A cross-sectional study comparing pre-bedtime and bedtime BP measurements found that the former correlated best with morning reading. BP measured within 2 h post-shower or 8 h after alcohol intake was significantly lower.[69] Therefore, nocturnal activity should be considered when measuring nighttime BP. If pre-dinner measurements are impractical, bedtime or pre-dinner readings are recommended. If patients are prescribed anti-hypertensives at bedtime, BP measurements should be conducted before taking the medication.

Notably, some guidelines have suggested discarding first-day BP measurements because they tend to be higher, potentially diminishing the accuracy of the results. However, current research shows that first-day measurements do not significantly impact cardiovascular risk prediction or diagnostic precision, particularly when a 7-day measurement regimen is used.[70,71] The 7-day HBPM can commence on any day of the week, although a 3-day method may yield variability owing to lower weekend and higher Monday readings, especially for employed individuals.[72]

Clinical Question 6: What Kinds of Non-Pharmacological Interventions are Recommended in Patients with Hypertension?

Recommendations

Lifestyle interventions, including healthy diet, exercise, stress reduction, weight loss, alcohol restriction and smoking cessation, and comprehensive lifestyle interventions, are recommended for all patients with hypertension (2B).

Evidence and rationale

Non-pharmacological interventions are the cornerstone of hypertension treatment. All patients with hypertension are recommended non-pharmacological interventions, with previous studies confirming their effectiveness. Moreover, the national and international guidelines on hypertension recommend non-pharmacological interventions.[6,29,73–77] The intervention modalities included a healthy diet, exercise, stress reduction, weight loss, alcohol restriction and smoking cessation, and comprehensive lifestyle intervention, as detailed in Table 3.

A systematic review showed that patients with an SBP 130–139 mmHg and/or a DBP 80–89 mmHg, as well as those with a BP ≥140/90 mmHg, benefit from the Dietary Approaches to Stop Hypertension (DASH) diet, aerobic exercise, isometric training, low sodium and high potassium salt consumption, salt restriction, respiratory control, and meditation to reduce both SBP and DBP, compared with those who maintain their routine lifestyle. Among them, the DASH diet is superior to the other non-pharmacological interventions (SBP: weighted mean difference [WMD] = 6.97 mmHg, 95% CI: 4.50–9.47 mmHg; DBP: WMD = 3.54 mmHg, 95% CI: 1.80–5.28 mmHg). In addition, yoga, resistance strength exercises, alcohol restriction, and progressive muscle relaxation have anti-hypertensive effects. Among overweight and obese individuals, the BP lowering effects of a hypocaloric diet (SBP: WMD = 6.50 mmHg, 95% CI: 2.78–10.17 mmHg; DBP: WMD = 4.56 mmHg, 95% CI: 2.22–6.89 mmHg) and combined exercise (SBP: WMD = 4.12 mmHg, 95% CI: 1.22–7.03 mmHg; DBP: WMD = 3.35 mmHg, 95% CI: 1.41–5.32 mmHg) were superior to those of exercise alone.[73]

As a combined intervention, comprehensive lifestyle modifications showed optimal efficacy in reducing the SBP and DBP.[73,74] A systematic review showed that the combination of a healthy diet and physical activity presents the best performance in reducing BP compared with the usual care group (SBP = −9.88 mmHg, 95% CI: −13.32 mmHg to −6.44 mmHg; DBP = −6.28 mmHg, 95% CI: −8.78 mmHg to −3.78 mmHg). The second is a combined intervention of healthy eating, physical activity, smoking cessation, and alcohol restriction (SBP = −6.58 mmHg, 95% CI:

Table 3: Non-pharmacological interventions for patients with hypertension.

Intervention	Dose
Dietary interventions	• DASH: adherence to consume a diet rich in fruits, vegetables, whole grains, low sodium, and low-fat dairy products
	• Consumption of an alternative salt or low sodium potassium-rich diet: Cooking with alternative salt or consumption of alternative salt foods; a sodium salt intake of <5 g/day (around one teaspoon) is recommended and the optimal goal is <1.5 g/day, and the recommended potassium intake is 3500–4700 mg/day
Exercise interventions	• Moderate intensity aerobic exercise: 30–60 min/day, 5–7 days/week to achieve 50–70% of maximal heart rate
	• Dynamic resistance: 90–150 min/week, 50–80% 1 rep maximum weight, 6 exercises, 3 sets/exercise, 10 repetitions/set
	• Isometric resistance: 4 min × 2 min (hand grip), 1 min rest between exercises, 3 sessions/week
	• Tai Chi and Qigong can also assist with BP reduction
Stress reduction	• Respiratory control: Slow regular breathing (preferably with the aid of specialized breathing equipment) performed daily at bedtime, with a target respiratory rate <10 breaths/min, 15 min/time, >40 min/week
	• Meditation: 20 min each time, 2 times/day
	• Yoga: 3 days/week, 30 min/day
Weight loss*	• Energy deficit of 500–750 kcal/day
	• Mode of exercise: Choose moderate to high intensity aerobic exercise, 30–60 min/day, 5–7 days/week, 60–90% HRR
	• Best goal is ideal body weight, BMI 18.5–23.9 kg/m^2
	• Waist: men <90 cm, women <80 cm
Alcohol restriction and smoking cessation	• No smoking, quit smoking thoroughly, avoid passive smoking
	• In individuals who drink alcohol, reduce alcohol to: men ≤20 g/day, women ≤10 g/day
	• Preferably abstain from alcohol and avoid binge drinking
Comprehensive lifestyle modification	• Combined diet and exercise interventions are the most effective non-pharmacological interventions that minimize BP when performed in parallel with other lifestyle interventions

*Weight loss with a combined hypocaloric diet and exercise are recommended in people who are overweight or obese; 1 kcal = 4.2 kJ. BP: Blood pressure; BMI: Body mass index; DASH: Dietary Approaches to Stop Hypertension; HRR: Heart rate reserve.

–10.46 mmHg to –2.70 mmHg; DBP = –4.09 mmHg, 95% CI: –7.13 mmHg to –1.05 mmHg).[74]

Clinical Question 7: Is it Recommended for Chinese Patients with Hypertension to Use a Low Sodium Salt Added with 25% Potassium Chloride instead of 99% Sodium Chloride?

Recommendations

In Chinese patients with hypertension, using a low-sodium salt instead of common salt is recommended (1B).

Reducing the intake of sodium to <2000 mg/day (about 5 g sodium chloride) is recommended (1B).

Targeting potassium intake between 3500 mg/day and 4700 mg/day is recommended (2B).

Evidence and rationale

Excessive sodium and insufficient potassium intakes are important risk factors for hypertension. Reducing the sodium intake and increasing the potassium intake can effectively reduce BP.[78–80] The intake of dietary sodium by Chinese residents is relatively high, with an average intake of approximately 9.3 g/day.[81] Reducing sodium intake to <2000 mg/day (approximately 5 g of sodium chloride) is recommended to prevent the development of hypertension.[82]

In traditional Chinese dietary patterns, approximately 3/4 of sodium intake comes from home-cooking salt, and reducing the sodium content in home-cooking salt is an important strategy for anti-hypertensive treatment.[83] The results from the Salt Substitute and Stroke Study (SSaSS) trial, which was based on the Chinese population, showed that compared with the regular salt (100% sodium chloride) diet group, the risk was decreased by 14% (relative risk [RR] = 0.86, 95% CI: 0.77–0.96) for stroke, by 13% (RR = 0.87, 95% CI: 0.80–0.94) for CVD, and by 12% (RR = 0.88, 95% CI: 0.82–0.95) for all-cause death in the low-sodium salt (75% sodium chloride and 25% potassium chloride) diet group.[84] Based on the DECIDE-salt study of the elderly Chinese results found that a salt substitution diet can reduce the elderly SBP by 7.1 (95% CI: –10.5 to –3.8) mmHg and significantly reduce the risk of cardiovascular events (HR = 0.6, 95% CI: 0.82–0.96).[85] Because salt substitutes with low sodium and high potassium pose a risk of hyperkalemia, evaluating renal function and medical therapy before salt substitution is recommended. Patients with mild renal insufficiency or those on drugs that can elevate blood potassium should be monitored regularly, with the blood potassium level checked, whereas patients with chronic kidney disease (CKD) of stage ≥3 should avoid the salt substitute strategy of low sodium and rich potassium.

A previous study showed that when potassium intake was 90–120 mmol/day (approximately 3500–4700 mg/day), SBP was decreased by 7.16 (95% CI: −1.91 to −12.41) mmHg.[86] Potassium intake is related to the risk of stroke, with the nadir risk at a potassium intake of 90 mmol/day (about 3500 mg/day) (RR = 0.78, 95% CI: 0.70–0.86) compared with other dose groups.[87] The level of dietary potassium in Chinese residents is low, and enriching potassium intake is recommended, with a target of 3500–4700 mg/day. Potassium-rich foods, including fresh fruits and vegetables, low-fat dairy products, nuts, and beans, are recommended.

The ratio of urinary sodium to potassium is more closely related to BP than urinary sodium or potassium levels measured separately. The reduction in this ratio is associated with a lowering of BP in adults.[88] Besides, some studies have indicated that the reduction of this ratio is also related to the reduction of the risk of CVDs and stroke.[89] Hence, it is recommended as one of the reference indicators for evaluating the risk of hypertension and its treatment effect.

Clinical Question 8: What Exercise Prescription (Including Type, Time, and Frequency) is Recommended for Hypertension?

Recommendations

Patients with high BP (SBP <160 mmHg and DBP <100 mmHg) should engage in 5–7 days (30–60 min/time) per week of moderate-to-high intensity aerobic exercise and 2–3 times/week of resistance exercise (1B).

Patients with high BP who cannot reach the above recommendation are suggested to increase physical activities as much as possible (1B).

Evidence and rationale

Regular exercise or increased physical activity can help control BP and reduce the risk of cardiovascular mortality.[90] A scientific statement from the 2021 American Heart Association (AHA)[91] and 2020 European Society of Cardiology (ESC) Guidelines on sports cardiology[92] and exercise in patients with CVD suggested that physical activity should be taken as the primary prevention for hypertension and recommended 5–7 days (at least 30 min/time) per week of moderate-to-high intensity aerobic exercise and 2–3 times/week of resistance exercise.

Based on a systematic review, a combination of aerobic and resistance exercises was more effective in lowering SBP, with durations of 30–45 min each time and frequencies of 3–5 times/week. Moderate intensity was better than low or high intensity.[93] Comparing the effects of moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) on BP in individuals with hypertension, both HIIT and MICT promoted a reduction in SBP in adults with hypertension, with HIIT showing a greater magnitude of DBP reduction.[94] Furthermore, all exercise types were associated with better mental health than no exercise.[95] Meanwhile, the largest associations were observed for popular team sports, cycling, and aerobic activities. Significant reductions in all-cause mortality were observed in the cycling, swimming, racquet sports, and aerobic groups. Racquet sports participation was associated with a significantly reduced risk of all-cause mortality of 47% (HR = 0.53, 95% CI: 0.40–0.69), which was considered to be the most cost-effective type of exercise.[96]

To ensure the safety of exercise for patients with hypertension, doctors should conduct a comprehensive assessment and classification first when they recommend exercise interventions to these patients, then clarify their exercise contraindications and advise them to increase exercise intensity and amount gradually in accordance with the principle of "start low and go slow". To patients with well-controlled BP, moderate intensity (i.e., 40–59% heart rate reserve [HRR]) or high intensity (i.e., 60–75% HRR) aerobic exercise is recommended. Notably, the HRR method for prescribing exercise intensity using HR is: Target HR (THR) = (HRmax − HRrest) × A% intensity desired + HRrest. If A is 70, then THR = (HR max − HR rest) × 70% + HRrest.[97] High-intensity aerobic and resistance exercises are not recommended for patients with uncontrolled BP and/or target organ damage and/or cardiovascular clinical complications and can be guided to increase physical activity as much as possible according to their body conditions. Aerobic exercises, including cycling, swimming, brisk walking, running, badminton, table tennis, gymnastics, and team sports, are recommended for patients with hypertension. Resistance exercises using dumbbells, small sandbags, and resistance bands are also recommended. Bowing the head or holding the breath should be avoided.

Clinical Question 9: Should Drugs or Surgery be Actively Recommended When Comprehensive Lifestyle Intervention is Ineffective in Weight Control for Obese Patients with Hypertension?

Recommendations

Patients with hypertension aged 18–65 years with body mass index (BMI) ≥28 kg/m^2 may consider using drugs validated in clinical trials to control weight if comprehensive lifestyle interventions fail (2B).

Metabolic surgery can be considered in hypertensive patients aged 18–65 years with BMI ≥35.0 kg/m^2 to control weight if non-operative intervention fails (2B).

Evidence and rationale

Overweight and obesity are important risk factors for hypertension and significantly increase the risk of death worldwide.[98] Overweight or obese patients with hypertension are advised to lose weight and maintain their BMI between 18.5 kg/m^2 and 23.9 kg/m^2.[99]

Traditional weight-loss drugs (such as orlistat and phentermine) can reduce weight and BP in patients with

hypertension; however, they have many adverse side effects.[100] Recently, new weight-loss drugs, the glucagon-like peptide-1 receptor agonist (GLP-1RA), including liraglutide and semaglutide, as well as the glucose-dependent insulinotropic peptide/GLP-1 dual receptor agonist tirzepatide, have been approved in multiple countries for weight management in obese or overweight adults. Recently, the National Medical Products Administration (NMPA) in China also approved the use of semaglutide for weight loss.[101–104] The recently published results of the Tirzepatide for Weight Reduction in Chinese Adults With Obesity (SURMOUNT-CN) Phase III clinical trial of tirzepatide demonstrated significant weight loss in obese or overweight Chinese adults.[105] The Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT) study showed that semaglutide not only effectively reduced weight but also significantly lowered the risk of major cardiovascular endpoint events by 20% (HR: 0.80, 95% CI: 0.72–0.90), with good safety and tolerability.[106] Consequently, the United States Food and Drug Administration (FDA) approved a new indication for the use of semaglutide to reduce the risk of cardiovascular death, heart attack, and stroke in adults with CVD who are either obese or overweight. Semaglutide should be administered in addition to a reduced-calorie diet and increased physical activity. This provides a new option for overweight or obese patients with hypertension. For patients with severe obesity, surgical treatment is an effective method for maintaining long-term weight stability, reducing complications, and improving the quality of life. Some studies have shown that metabolic surgery can effectively reduce SBP (WMD = −3.937 mmHg, 95% CI: −6.000 mmHg to −1.875 mmHg) and DBP (WMD = −2.690 mmHg, 95% CI: −3.994 mmHg to −1.385 mmHg), and improve metabolic syndrome.[107]

In view of the adverse reactions to weight loss drugs and the complications of metabolic surgery, the weight loss strategy should first adopt comprehensive lifestyle interventions, including health education, diet control, exercise, and behavioral interventions. When these measures are ineffective, drugs or bariatric surgery may be considered. Hypertensive patients with a BMI ≥35.0 kg/m^2 may consider metabolic surgery according to their wishes when weight control is poor after non-surgical treatment.[108–110]

Clinical Question 10: How can the Timing of Initiating Anti-Hypertensive Drug Treatment be Determined based on Cardiovascular Risk Stratification?

Recommendations

Initiation of pharmacological anti-hypertensive treatment in patients with high risk of CVD, detailed in the following three scenarios: (1) an SBP ≥140 mmHg and/or a DBP ≥90 mmHg, immediate initiation of anti-hypertensive drug therapy is recommended (1B); (2) an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg with clinical comorbidities, it is recommended to initiate anti-hypertensive medication treatment (1B); (3) an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg with target organ damage (GPS) or ≥3 cardiovascular risk factors, anti-hypertensive medication can be initiated (2C).

Cardiovascular risk stratified as a non-high risk; that is, patients with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg with 0–2 cardiovascular risk factors can undergo lifestyle intervention for 3–6 months. If SBP remains ≥130 mmHg and/or DBP ≥80 mmHg, consider initiating anti-hypertensive medication (2C).

Evidence and rationale

For patients with an SBP of ≥140 mmHg and/or a DBP of ≥90 mmHg, a fixed degree of pharmacological BP lowering is similarly effective for the primary and secondary prevention of major cardiovascular events and death.[21,111] Cardiovascular risk assessment is not a prerequisite for drug therapy decisions in all patients with hypertension. For patients with an SBP ≥140 mmHg and/or a DBP ≥90 mmHg, a cardiovascular risk assessment may be performed concurrently with or after the initiation of pharmacological therapy to avoid delaying the timing of treatment. For patients with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg, regardless of whether they have cardiovascular comorbidities, aggressive BP reduction significantly reduces the risk of cardiovascular events and mortality.[21,22] The extent of mortality risk reduction is related to the degree of blood reduction.[112] The relative reduction in cardiovascular risk from aggressive BP management is consistently observed even in patients with pre-existing CVD and is also evident in those with baseline SBP <130 mmHg.

For patients with hypertension and diabetes, evidence of the benefits of anti-hypertensive drug treatment is not entirely consistent across various systematic reviews.[113–115] The results of the RCT (Action to Control Cardiovascular Risk in Diabetes [ACCORD] study) showed that although the difference in event benefit for the primary cardiovascular endpoint of aggressive antihypertension compared with conventional antihypertension was not statistically significant (HR = 0.88, 95% CI: 0.73–1.06), the risk of the secondary endpoint, stroke, decreased by 41%.[113] Both the Systolic Blood Pressure Intervention Study (SPRINT)[114] and Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients (STEP) study[115] showed significant effects of aggressive BP lowering on reducing cardiovascular event risks (the former did not include patients with diabetes, while the latter included approximately 20% of patients with diabetes). Because the absolute benefits of BP-lowering therapy are related to the baseline cardiovascular risk level of patients, it is more reasonable to aggressively lower BP to <130/80 mmHg for patients with hypertension and diabetes, considering their higher baseline cardiovascular risks.

Patients with an SBP 130–139 mmHg and/or a DBP 80–89 mmHg, and with HMOD, are at a high risk of cardiovascular outcomes, and intensive control of BP is beneficial for preventing the progression of target organ damage. As for patients with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg and with

≥3 cardiovascular risk factors, there are not enough outcome data to support the initiation of drug therapy. However, the results of the SPRINT study showed that aggressive BP lowering in patients with an SBP of 130–180 mmHg and increased cardiovascular risk resulted in a further 25% reduction in the risk of cardiovascular events compared with conventional BP lowering.[114] The STEP study also found similar benefits of intensive BP reduction in elderly patients with hypertension aged 60–80 years.[115] We recommend that anti-hypertensive drug treatment should be considered individually for these patients.

Although lifestyle interventions have a certain effect on BP control in low-risk patients with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg and a 10-year ASCVD risk of <10%, it is difficult to maintain diet, exercise intervention, and others at stable targets for a long time. At the same time, considering that people with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg have a significantly higher risk of cardiovascular events than those with BP <130/80 mmHg,[116–118] drug treatment can effectively delay the progression of such patients to a higher BP level.[119–121] Therefore, this guideline proposes that for patients with an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg and with 0–2 cardiovascular risk factors, if the BP is still ≥130/80 mmHg after 3–6 months of lifestyle intervention, initiation of anti-hypertensive drug treatment can also be considered. However, high-quality studies are required to clarify whether anti-hypertensive drug treatment can bring more benefits to these patients.

Notably, there is a lack of direct evidence for the recommendation of the timing of initiating anti-hypertensive drugs in patients with a DBP of 80–89 mmHg. In the Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC) study, it was found that for every 3 mmHg decrease in DBP, the risk of MACEs in patients with hypertension of different age groups was reduced, and the magnitudes were similar.[22] High-quality studies are needed to confirm whether anti-hypertensive drug treatment benefits this patient group.

Clinical Question 11: How should Target Values for Blood Pressure Control be Set for Different Hypertensive Patients?

Clinical question 11-1: What is the blood pressure targets in patients with hypertension without clinical comorbidities and aged <65 years?

Recommendations

It is recommended that the blood pressure (BP) target value for hypertensive patients without clinical comorbidities and aged <65 years be <130/80 mmHg (2B).

Evidence and rationale

The BPLTTC systematic review showed that a 5 mmHg reduction in SBP reduced the risk of MACEs by 10%, regardless of the presence of prior CVD (HR = 0.90, 95% CI: 0.88–0.92). MACEs include fatal or non-fatal stroke, fatal or non-fatal myocardial infarction, ischemic heart disease, and fatal or heart failure (HF) requiring hospitalization.[21] Compared to maintaining BP at <140/90 mmHg, a target of <130/80 mmHg could reduce the risk of left ventricular hypertrophy (odds ratio [OR] = 0.63, 95% CI: 0.43–0.91)[122] and cerebral hemorrhage (HR = 0.37, 95% CI: 0.15–0.95)[123] in patients with hypertension. The SPRINT study showed that controlling SBP at <120 mmHg was associated with a benefit in the mean survival time of 6 months to 3 years in patients with hypertension, as compared to controlling SBP at <140 mmHg.[124] The study also showed that a target SBP of <120 mmHg resulted in an increased risk of serious adverse events, including hypotension (HR = 1.67, P <0.01), syncope (HR = 1.33, P = 0.05), electrolyte abnormalities (HR = 1.35, P = 0.02), and acute renal impairment or failure (HR = 1.66, P < 0.01).[114] A recent open-cohort RCT of 33,995 individuals in China suggested that a control rate of 57% could be achieved after 18 months of intervention targeting 130/80 mmHg in the general community-dwelling population, confirming that antihypertensive regimens with 130/80 mmHg as the target in the community-dwelling general population were feasible.[125] Further studies showed that, after 36 months of intervention and follow-up, an intensified antihypertensive regimen resulted in a 33% reduction in the risk of cardiovascular events and a 30% reduction in the risk of cardiovascular death, while continuing to improve control rates with a target of 130/80 mmHg. Compared with the control group, despite the increased incidence of hypotension in the intervention group, no significant differences in injurious falls, symptomatic hypotension, or syncope were reported between the two randomization groups, confirming that intensified antihypertensive treatment was safe and effective in the community-dwelling general population.[126]

In addition, a secondary analysis of the CRHCP study showed that an intensive antihypertensive regimen (<130/80 mmHg) significantly reduced the risk of cardiovascular and cerebrovascular events in normotensive patients aged <60 years (HR = 0.64, 95% CI: 0.56–0.75).[127] It should be noted that clinicians should consider potential adverse effects, such as hypotension, syncope, electrolyte abnormalities, and acute kidney injury, when developing specific antihypertensive strategies for each patient with hypertension.

Clinical question 11-2: What is the target value for blood pressure control in patients with hypertension combined with atrial fibrillation?

Recommendations

For patients with hypertension combined with AF, the target BP is recommended to be <130/80 mmHg (2C).

Evidence and rationale

Hypertension is a common independent risk factor for AF, and more than 20% of AF cases can be attributed to hypertension.[128] Recent studies have suggested that intensive BP control can offer additional benefits to patients with both hypertension and AF. A *post hoc* analysis of the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) study showed that intensive BP lowering significantly reduced the risk of all-cause mortality, cardiovascular death, myocardial infarction, stroke, and hospitalization for HF in patients with diabetes and AF.[129] Moreover, an individual-level systematic review of 22 RCTs involving 188,570 participants demonstrated that a 5-mmHg reduction in SBP reduced the risk of MACEs by 9%. This benefit was similar between patients with and without AF (with AF: HR = 0.91, 95% CI: 0.83–1.00; without AF: HR = 0.91, 95% CI: 0.88–0.93).[130] Observational studies have consistently shown that patients with AF whose BP is controlled to <130/80 mmHg have a significantly lower risk of MACEs and dementia than do those with BP ≥130/80 mmHg.[131,132] Additionally, elevated BP (SBP ≥136 mmHg) is an independent risk factor for thromboembolism and major bleeding in patients with AF.[133] Therefore, it is reasonable to set a BP target of <130/80 mmHg for patients with hypertension and AF; however, large-scale RCTs to fully support this target are lacking. In clinical practice, the patient's age, comorbidities, and medication tolerance to ensure that BP is managed within an appropriate range for each individual.

Clinical question 11-3: What is the target value for blood pressure control in patients with hypertension combined with coronary heart disease (CHD)?

Recommendations

For hypertensive patients combined with CHD, a BP target of <130/80 mmHg is recommended (2B).

Evidence and rationale

Hypertension is a leading risk factor for CHD, and effective BP can reduce the risk of cardio-cerebrovascular morbidity and mortality in patients with hypertension and CHD. The 2017 ACC/AHA guidelines[6] and 2023 ESH guidelines[5] both recommended that the BP target in patients with hypertension and CHD should be <130/80 mmHg. However, domestic guidelines[134] recommend an antihypertensive target of <140/90 mmHg for patients with hypertension and CHD, which can be reduced to <130/80 mmHg if tolerated. However, attention should be paid to the fact that diastolic blood pressure (DBP) should not be reduced too much. Systematic evaluation showed that every 10-mmHg reduction in SBP was associated with significantly reduced risks of CHD (RR = 0.83, 95% CI: 0.78–0.88), MACEs (RR = 0.80, 95% CI: 0.77–0.83), and all-cause mortality (RR = 0.87, 95% CI: 0.84–0.91).[112] Patients with a mean achieved SBP of 120–124 mmHg had a lower risk of MACEs (HR = 0.71, 95% CI: 0.60–0.83) and all-cause mortality (HR = 0.73, 95% CI: 0.58–0.93),[135] as compared to patients with a mean achieved SBP of 130–134 mmHg. Thus, the current guidelines recommend a BP target of <130/80 mmHg for patients with hypertension and CHD. Nevertheless, this guideline does not recommend a lower limit for the BP control target in patients with hypertension and CHD, since the current relevant clinical evidence derived from observational studies has shown contradictory results.[136,137]

Notably, the BP target should be comprehensively evaluated after considering both the individual situation and tolerance of patients with CHD with HF, asthenia, or senescence, and a BP lower than 130/80 mmHg should be avoided.

Clinical question 11-4: What is the target value for blood pressure control in patients with hypertension combined with heart failure?

Recommendations

A target BP control value of <130/80 mmHg is recommended for hypertensive patients with reduced ejection fraction as well as preserved ejection fraction in cardiac failure (2B).

Evidence and rationale

Hypertension is the major cause of HF. BP management is a pivotal therapeutic strategy for improving the prognosis of cardiovascular outcomes in patients with hypertension and HF. A target of <130/80 mmHg has been recommended by most current guidelines for hypertension with chronic HF with reduced ejection fraction (HFrEF).[6,30,135,138] However, the BP targets of patients with hypertension and HF with preserved ejection fraction (HFpEF) are not clearly recommended in current guidelines, and the relevant evidence-based medicine is also lacking.

A review of a large-scale meta-analysis published in Lancet in 2016 suggested that a 10 mmHg reduction in SBP can significantly reduce the incidence of HF (RR = 0.72, 95% CI: 0.67–0.88), MACEs (RR = 0.80, 95% CI: 0.77–0.83), and all-cause mortality (RR = 0.87, 95% CI: 0.84–0.91) in patients with hypertension.[112] A systematic review published in 2019 showed that SBP ≤140 mmHg was associated with a significantly lower risk of HF, particularly in patients aged 65 years or older who do not have diabetes.[139] A meta-analysis published in 2019 demonstrated that the hospitalization rate for HF in the intervention group (134.7–130.2 mmHg) was lower than that in the control group (134.4–133.3 mmHg, RR = 0.89, 95% CI: 0.82–0.97).[140] Moreover, a decrease of 3–130 mmHg in SBP may be related to a reduction in HF hospitalization in patients with HFpEF.

A BP target of <130/80 mmHg is recommended in patients with hypertension and HF (including both HFrEF and HFpEF) to improve long-term prognosis and reduce the

risk of cardiovascular events. However, considering that a lower BP may affect long-term prognosis, the lower limit remains unclear in patients with HF. In clinical practice, BP should be adjusted according to the status and tolerance of the individual patient.

Clinical question 11-5: What is the target value for blood pressure control in patients with hypertension combined with diabetes?

Recommendations

In hypertensive patients combined with diabetes, a target of SBP <130 mmHg (2C) and DBP <80 mmHg (GPS) is recommended.

Evidence and rationale

Hypertension complicated by diabetes can severely threaten the cardiovascular system; increase the risk of myocardial infarction, stroke, and all-cause mortality; and increase the risk of HF, kidney disease, and microvascular events.[141] BP lowering, which decreases the risk of myocardial infarction, HF, and microangiopathy, is an important treatment strategy for patients with hypertension complicated by diabetes.[142,143] ASCVD risk assessment was introduced to identify individual targets for BP reduction.[142,143] The 2024 American Diabetes Association in Medical Care Standards in Diabetes recommended that patients with diabetes and hypertension who are at high cardiovascular risk (suffer from ASCVD or risk of 10 years, ASCVD ≥10%) should lower their BP to <130/80 mmHg, provided that it is safe to achieve their BP target.[142] A meta-analysis has shown that, in adults with diabetes and elevated SBP, an intensive SBP target of <120–140 mmHg decreased the risk of diabetes-related mortality (RR = 0.60, 95% CI: 0.50–0.92) and fatal (RR = 0.41, 95% CI: 0.20–0.84) or non-fatal stroke (RR = 0.60, 95% CI: 0.43–0.83). Moreover, in patients with diabetes who have an elevated DBP (90 mmHg), an intensive treatment with a DBP target of 80 mmHg decreased the risk of MACEs.[144] A *post hoc* analysis of two randomized trials showed that, in patients with diabetes whose SBP ranged from 130 mmHg to 180 mmHg, antihypertensive therapy (target SBP of <120 mmHg) decreased the risk of the primary composite end-point (HR = 0.82, 95% CI: 0.73–0.93), including unstable angina pectoris, myocardial infarction, acute HF, stroke, and cardiovascular death.[145] The diastolic blood pressure-lowering target goal for patients with hypertension combined with diabetes mellitus, combined with the current evidence and referring to the recommendations of existing domestic and foreign guidelines,[4,6,29,30,134,136] is suggested to be <80 mmHg.

Clinicians should focus on comprehensive risk factor management, including BP and glucose control, lipid-lowering therapy, and antithrombotic therapy, in patients with hypertension and diabetes to reduce the risk of ASCVD. Furthermore, potential adverse reactions, such as hypotension, syncope, and falls, should be considered. For older and weak patients, blood perfusion of important target organs should be considered, and the BP target should be appropriately raised to improve their quality of life.[142] For patients with diabetes complicated with CHD, particularly those with acute coronary syndrome, the BP control target also needs to be increased appropriately.[146]

Clinical question 11-6: What is the optimal blood pressure target in older patients with hypertension?

Recommendations

In older patients (aged 65–79 years) with hypertension, a BP target of <130/80 mmHg is recommended (2B).

In very old patients (≥80 years) with hypertension, if well-tolerated, lowering the office SBP to 130–139 mmHg can be considered (GPS).

Evidence and rationale

Hypertension is prevalent among older individuals, with a prevalence exceeding 50%.[147] The optimal BP target for older patients with hypertension has been hotly debated.[3,30,148] Recently, mounting evidence indicated that older patients may benefit additionally from intensified SBP lowering. In the SPRINT trial, intensive SBP lowering (<120 mmHg) *vs.* standard SBP lowering (<140 mmHg) was associated with 20% and 37% reduction in the risk of composite cardiovascular outcomes among individuals aged 50–75 years and ≥75 years, respectively.[114] In 2021, BPLTTC pooled 358,707 subjects from 51 RCTs and categorized them into five baseline age groups (<55 years, 55–64 years, 65–74 years, 75–84 years, and ≥85 years). Achieving a 5 mmHg reduction in SBP reduced MACE (fatal or non-fatal stroke, fatal or non-fatal myocardial infarction or ischemic heart disease, or HF causing death or requiring hospital admission) risks by 18%, 9%, 9%, and 9% in the first four age groups, respectively (i.e., $HR_{<55}$ = 0.82, 95% CI: 0.76–0.88; $HR_{55–64}$ = 0.91, 95% CI: 0.88–0.95; $HR_{65–74}$ = 0.91, 95% CI: 0.88–0.95; $HR_{75–84}$ = 0.91, 95% CI: 0.87–0.96). Similar patterns of proportional risk reduction were observed for a 3 mmHg reduction in DBP.[22] The STEP trial, which was based on the Chinese population, provided strong clinical evidence supporting intensive antihypertensive therapy.[115] In patients aged 60–80 years with hypertension, the risk of MACE (a composite outcome of stroke, acute coronary syndrome, acute decompensated HF, coronary artery revascularization, AF, or cardiovascular death) was significantly lower (HR = 0.74, 95% CI: 0.60–0.92) in patients assigned intensive treatment (SBP target, 110 mmHg to <130 mmHg) than in those assigned standard treatment (130 mmHg to <150 mmHg). Of note, the risk of safety outcomes (including dizziness, headache, syncope, fracture, vascular edema, cough, and urticaria), except for hypotension, was comparable (2.6% *vs.* 3.4%, P = 0.03) between treatment groups. Although neither the SPRINT[114] nor the STEP[115] trial included hypotension-related adverse events as primary outcomes, their primary composite end-points included both hypertension- and hypotension-related adverse effects. For

patients aged >80 years, solid clinical evidence addressing the optimal BP target remains limited, and recommendations are based on existing guidelines and expert opinions.

For older patients with hypertension who are in poor general condition, have cognitive dysfunction, fragility, or limited life expectancy, individualized BP targets should be customized according to their personal situation.[149,150] Additionally, antihypertensive drug treatment in older patients needs to involve increased monitoring of adverse reactions and tolerance, and should reduce the intensity of treatment when necessary.[6]

Clinical question 11-7: What is the recommended target value for blood pressure control in patients with hypertension and acute hemorrhagic stroke?

Recommendations

For hypertensive patients with acute hemorrhagic stroke, BP is recommended to be lowered in the acute phase and the SBP should be maintained at 130–140 mmHg (2C).

Evidence and rationale

It has been recommended that patients with hypertension complicated by intracerebral hemorrhage (ICH) receive antihypertensive treatment in the acute stage and that BP should be controlled within a certain range. Current foreign and domestic guidelines on hypertension and stroke are controversial regarding the recommended BP targets in the acute stage of ICH. The 2019 National Institute for Health and Care Excellence (NICE) guideline in the UK recommend that it is safe to control SBP within 130–140 mmHg during the acute stage of ICH. However, further verification is needed to determine whether functional outcomes improve.[151] The recently published Intensive Ambulance-Delivered Blood-Pressure Reduction in Hyperacute Stroke Trial (INTERACT4) study involved ultra-early BP lowering in an ambulance in patients with suspected acute stroke. Although the results of this study do not conclusively confirm that ultra-early BP reduction is associated with functional outcomes in patients with acute stroke, targeting an ultra-early SBP target of 130–140 mmHg in patients experiencing acute hemorrhagic stroke significantly reduces the risk of poor outcomes.[152] On the other hand, the 2024 ESC Guidelines on Hypertension suggest that SBP in patients with cerebral hemorrhage should be limited to 140–160 mmHg to prevent hematoma expansion and improve functional prognosis; however, overly rapid reductions in SBP of more than 70 mmHg are thought to be associated with renal impairment and early neurological deterioration.[3] These different recommendations may be due to the different sources of evidence. Patients admitted to hospitals with SBP >220 mmHg generally require strict BP control by default; therefore, they are rarely included in clinical studies. There is no clear evidence on the safety and efficacy of antihypertensive treatments in these patients. Recent systematic reviews and RCTs support the need for antihypertensive treatment in the acute phase of hypertension complicated by ICH; however, BP must be controlled within a certain range. A secondary analysis of the ATACH2 trial found an increased incidence of adverse cardiac and renal events with an SBP target of below 130 mmHg.[153] Therefore, combined with clinical practice experience, 130–140 mmHg may be a reasonable SBP range in the acute stage of ICH. More accurate BP targets still need to be confirmed by further RCTs.

In clinical antihypertensive treatment for the acute stage of ICH, close attention should be paid to the patient's history of hypertension, baseline BP, elevated intracranial pressure, and BP at admission. After excluding contraindications, the appropriate drugs should be selected for prudent antihypertensive treatment. During antihypertensive treatment, BP should be closely monitored, and vital signs should be considered, avoiding further deterioration of neurological function due to excessive BP variations.

Clinical question 11-8: Above which blood pressure level should antihypertensive therapy be initiated in patients with hypertension combined with acute ischemic stroke (AIS)?

Recommendations

In AIS patients not receiving intravenous thrombolysis or endovascular treatment (EVT), antihypertensive treatment is recommended to be initiated with SBP ≥220 mmHg and/or DBP ≥120 mmHg (2C).

For patients with AIS who are scheduled for intravenous thrombolysis and EVT, BP should be controlled within ≤185/110 mmHg before treatment (2C).

For patients with AIS who have undergone EVT and achieved successful recanalization, early intensive antihypertensive therapy should be avoided (1B).

Evidence and rationale

Consensus regarding the strategy for BP control in patients with AIS during the acute phase is lacking. AIS is often complicated by hypertension, which is associated with unfavorable outcomes, such as early stroke recurrence.[154] Many studies have reported a U-shaped relationship between BP and outcomes in patients with AIS.[155] Both too low and too high will lead to unfavorable outcomes. Some studies have found that large BP variability also leads to unfavorable outcomes, indicating that moderate antihypertensive treatment may be needed when BP is too high in the acute stage of AIS. An RCT involving patients with baseline BP <220/120 mmHg did not show a difference in outcomes between antihypertensive treatment and placebo, whereas in previous studies,[156] patients with BP ≥220/120 mmHg were considered to be above the upper limit of cerebral blood flow regulation and required antihypertensive treatment by default. Therefore, some guidelines recommend initiating antihypertensive treatment only when BP is ≥220/120 mmHg.[3,157] A meta-analysis showed that antihypertensive treatment within 72 h of stroke onset

did not improve outcome (90-day modified Rankin score: OR = 1.01, 95% CI: 0.94–1.08, $P = 0.75$), and could not reduce the risk of death (OR = 1.03, 95% CI: 0.92–1.15, $P = 0.59$).[158] Therefore, there is no clear evidence of the safety, efficacy, or reasonable targets of antihypertensive treatment. On the basis of current studies and clinical experience, patients with AIS with SBP ≥220 mmHg and/or DBP ≥120 mmHg are recommended to receive antihypertensive treatment when intravenous thrombolysis and EVT are not performed.

The effect of BP on prognosis is also related to the vascular recanalization status.[159] At present, the view that BP must be controlled in patients with AIS before thrombolysis is relatively consistent; however, evidence to support a target value is lacking. The results from a meta-analysis showed that, for every 10 mmHg increase in baseline SBP, the odds of a favorable outcome after thrombolysis decreased by 7% (OR = 0.93, 95% CI: 0.91–0.94), and the risk of ICH increased by 12% (OR = 1.12, 95% CI: 1.08–1.16).[160] Since patients with SBP >185 mmHg or DBP >110 mmHg were generally excluded from most previous RCTs on recombinant tissue plasminogen activators, some guidelines recommend thrombolytic therapy if the BP is below 185/110 mmHg. However, some studies have shown that prethrombolysis BP (<185/110 mmHg or not) is not associated with the outcome,[161] suggesting that according to the current guidelines, it may be safe to maintain prethrombolysis BP below 185/110 mmHg without increasing the risk of unfavorable outcomes, but the exact target BP requires further evidence. A previous study has shown that a higher BP on admission is associated with a lower rate of recanalization and worse clinical outcomes in patients undergoing EVT,[162] suggesting that BP control before recanalization therapy may reduce the incidence of unfavorable outcomes. Current guidelines[163] and consensus indicate that many RCTs[164–167] regarding EVT have excluded patients with BP >185/110 mmHg. Until more definitive results are published, it may be reasonable to use a BP target of ≤185/110 mmHg before EVT.

Regarding the use of BP lowering in patients with acute stroke who have undergone EVT, the recently published Intensive Blood Pressure Control after Endovascular Thrombectomy for Acute Ischaemic Stroke (ENCHANTED2/MT)[168] and OPTIMAL-blood pressure[169] studies showed that intensive BP lowering was associated with poor outcomes; therefore, early intensive BP lowering should be avoided after recanalization in patients with AIS.

Currently, clear guidance regarding the benefits and target values for lowering BP in patients with AIS during the acute phase is lacking. From the current evidence, it can be deduced that both a high baseline BP and large BP variability may lead to unfavorable outcomes. Therefore, careful and appropriate BP management strategies should be formulated according to the individual patient condition and their recanalization status. Continuous BP monitoring is necessary during the acute phase of AIS.

Clinical question 11-9: What is the blood pressure target for hypertensive patients with stable stroke (including hemorrhagic and ischemic stroke)?

Recommendations

For hypertensive patients with stable stroke, a BP target of <130/80 mmHg is recommended to prevent stroke recurrence (1A).

Evidence and rationale

In terms of BP control targets for stroke patients with stable status, the recommendations from hypertension guidelines of the past 5 years are consistent with stroke guidelines, which both recommending that hypertensive patients with a history of previous stroke (including hemorrhagic and ischemic stroke) should have BP maintained below 130/80 mmHg to reduce the risk of stroke recurrence and vascular events.[6,30,170] Both the Continue or Stop Post-Stroke Antihypertensives Collaborative Study (COSSACS)[171] and China Antihypertensive Trial in Acute Ischemic Stroke (CATIS)[172] studies have shown that starting or restarting antihypertensive treatment is associated with improved BP control after discharge; therefore, BP control in patients with previous stroke is considered to have certain clinical benefits. Recent systematic reviews have been consistent regarding SBP targets, with studies showing that, compared to SBP of 130–140 mmHg (9.2%, 95% CI: 6.9–12.1%) and SBP of >140 mmHg (11.7%, 95% CI: 9.4–14.3%), patients with an SBP <130 mmHg had a lower risk of stroke recurrence (8.3%, 95% CI: 7.0–9.8%, P <0.05).[173,174] With respect to DBP control targets, compared to a DBP of 85–90 mmHg (12.3%, 95% CI: 7.3– 20.1%) and DBP >90 mmHg (19.2%, 95% CI: 14.5–24.9%), patients with DBP <85 mmHg had a lower risk of stroke recurrence (11.9%, 95% CI: 9.2–15.1%, $P = 0.03$).[174] According to current guidelines, DBP should be maintained at <80 mmHg. In summary, patients with stable stroke should have long-term BP control, and BP control to <130/80 mmHg may be beneficial in reducing stroke recurrence.

Clinical question 11-10: What is the target blood pressure for non-dialysis chronic kidney disease (CKD) patients?

Recommendations

Non-dialysis CKD patients with urinary protein >300 mg/day whose office BP is consistently ≥140 mmHg systolic or ≥90 mmHg diastolic should be treated with a target BP of <130/80 mmHg, and a further reduced SBP of 120 mmHg, if tolerated (2B).

Non-dialysis CKD patients with urinary protein ≤300 mg/day whose office BP is consistently ≥140 mmHg systolic or ≥90 mmHg diastolic should be treated with a target of <140/90 mmHg, and a further reduced SBP of 130 mmHg, if tolerated (2B).

Evidence and rationale

The prevalence of CKD in China is 8.2%, affecting an estimated 82 million patients.[175] The prevalence of hypertension in non-dialysis CKD patients in China is 67.3%, which is significantly higher than that in the general population.[176] Hypertension is a major risk factor for the occurrence and development of CKD, and significantly increases the risk of CVD and death. Previous systematic reviews have shown that intensive antihypertensive treatment (BP <130/80 mmHg) resulted in an 18% risk reduction of composite endpoints in CKD patients (doubling of serum creatinine, 50% decline in glomerular filtration rate [GFR], or end-stage renal disease [ESRD]) (HR = 0.82, 95% CI: 0.68–0.98) and a 21% reduction in the risk of ESRD (HR = 0.79, 95% CI: 0.67–0.93). In subgroup analysis, intensive antihypertensive therapy did not improve renal outcomes in CKD patients without proteinuria, but it reduced the risk of renal failure in patients with proteinuria (RR = 0.76, 95% CI: 0.64–0.89). When proteinuria exceeds 300 mg/day, intensive antihypertensive treatment reduced the risk of composite endpoint events (50% [or 25 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$ decrease in GFR, kidney failure, or death]) in CKD patients (HR = 0.74, 95% CI: 0.56–0.99).[177,178] Among the overall population of the SPRINT, targeting an SBP <120 mmHg, as compared with <40 mmHg, showed a decreased risk of MACEs and all-cause death, but an increased risk of adverse events, such as acute kidney injury, incident CKD, hypotension, and electrolyte abnormality.[114,179] Among participants who had CKD at baseline, no significant benefits in primary cardiovascular and renal outcomes were noted.[114] In 2017, a systematic review, aiming to evaluate BP control goal of CKD patients without diabetes, revealed that compared with standard BP control (<140/90 mmHg), intensive BP control (<130/80 mmHg) did not show a significant difference on the annual rate of change in GFR (MD = 0.07 ($mL \cdot min^{-1} \cdot 1.73\ m^{-2}$)/year), composite renal outcome (creatinine doubling, 50% reduction in GFR, or ESRD, RR = 0.99, 95% CI: 0.81–1.21), or all-cause mortality (RR = 0.81, 95% CI: 0.64–1.02).[180] In addition, the pooled estimates showed an increased risk of dizziness with intensive BP-lowering treatment (RR = 1.13, 95% CI: 1.05–1.22). Therefore, intensive antihypertensive treatment may increase the risk of adverse events in patients with CKD.

In clinical practice, risks and benefits should be balanced according to tolerance and clinical characteristics and to individualized BP control targets for patients with CKD.

Clinical Question 12: Do Patients with Hypertension Need to Reach the Blood Pressure Standard within Four Weeks?

Recommendations

Hypertensive patients without clinical comorbidities and aged <65 years are recommended to achieve BP targets within 4 weeks (2D).

Evidence and rationale

The Physicians–Patients Survey found that both physicians and patients wanted to reach BP targets as soon as possible.[181] A retrospective study showed that total mortality in hypertensive patients was elevated with prolonged BP diagnosis–control time (D-C time), and those with a D-C time >90 days had a higher risk of all-cause mortality than did those with a D-C time of <30 days (HR = 1.153, 95% CI: 1.018–1.306).[182] The results of the Felodipine Event Reduction (FEVER) study showed that the risk of stroke (HR = 0.67, 95% CI: 0.52–0.86), cardiovascular events (HR = 0.61, 95% CI: 0.49–0.75), and all-cause mortality (HR = 0.55, 95% CI: 0.39–0.78) was significantly lower in patients who met the BP target than in those who did not meet the target, and the risk of stroke and cardiovascular events was significantly lower in those who met the BP target than in those who did not meet the target within 3–6 months, while there was no statistical significance in the risk of all-cause death.[183] However, in clinical practice, it takes much longer than four weeks for hypertensive patients to achieve good BP targets.[182,184] Based on evidence and patient preferences, this guideline recommends that hypertensive patients without clinical comorbidities and aged <65 years achieve BP targets within 4 weeks; however, the rate of BP lowering should not be too rapid in the elderly, frail, and patients with autonomic dysfunction or orthostatic hypotension (OH), so such patients can extend the time of BP targets according to the actual situation.[182]

Clinical question 13: How to Recommend Initiation of Antihypertensive Drug Therapy for Hypertensive Patients without Clinical Complications?

Recommendations

Angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), calcium-channel blockers (CCBs), and diuretics are recommended as first-line therapy in hypertensive patients without clinical complications (1B).

Evidence and rationale

For hypertensive patients without clinical complications, most guidelines recommend diuretics, ACE inhibitors, ARBs, and CCBs as the initial antihypertensive agents, while a few guidelines also recommend β-blockers as the first-line agents.[4–6,185]

In general, the clinical benefits of ARBs, ACE inhibitors, CCBs, diuretics, and β-blockers for patients with hypertension outweigh the potential risks. The results of a network meta-analysis indicated that, compared with placebo, ACE inhibitors were reported to be the most effective in reducing the risk of overall cardiovascular events, by 29% (RR = 0.71, 95% CI: 0.60–0.83) in patients with hypertension, followed by dihydropyridine CCBs (RR = 0.73, 95% CI: 0.64–0.84), diuretics (RR = 0.73, 95% CI: 0.62–0.85), ARBs (RR = 0.79, 95% CI: 0.67–0.94), and β-blockers (RR = 0.83, 95% CI: 0.70–0.98).[186] Additionally, diuretics provide the largest reduction of the risk of cardiovascular death

(RR = 0.78, 95% CI: 0.69–0.88), followed by ACE inhibitors (RR = 0.80, 95% CI: 0.70–0.91), dihydropyridine CCBs (RR = 0.80, 95% CI: 0.71–0.89), and ARBs (RR = 0.85, 95% CI: 0.74–0.97), while β-blockers failed to reduce the risk of cardiovascular death (RR = 0.99, 95% CI: 0.87–1.13).[186] To reduce the risk of all-cause mortality, both ACE inhibitors (RR = 0.83, 95% CI: 0.72–0.95) and diuretics (RR = 0.89, 95% CI: 0.82–0.97) were effective as compared to placebo.[187] Another meta-analysis showed that CCBs significantly reduced the risk of MACEs (RR = 0.84, 95% CI: 0.77–0.92), stroke (RR = 0.77, 95% CI: 0.67–0.88), and cardiovascular death (RR = 0.90, 95% CI: 0.81–0.99) as compared with β-blockers.[188] Currently, no evidence is available to support the efficacy of ARBs or β-blockers on all-cause mortality in patients with hypertension without clinical complications. Concerning safety, antihypertensive agents, including β-blockers and thiazide diuretics, increase the risk of discontinuing medication due to adverse effects in patients with elevated BP.[187] Furthermore, the results of a meta-analysis have indicated that, compared to β-blockers, calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), and thiazide diuretics can significantly reduce this risk.[189]

In conclusion, β-blockers are less effective than other antihypertensive drugs in improving clinical outcomes in patients with hypertension, and their safety is lower. Therefore, these guidelines do not recommend β-blockers as first-line antihypertensive drugs. However, for hypertensive patients with high heart rates and sympathetic nerve excitation, β-blockers can be considered for antihypertensive treatment. In clinical practice, one or more agents should be selected as the initial antihypertensive drug according to the individual characteristics of the patients and the pharmacology of the drug.

Clinical Question 14: When do Patients with Hypertension Need to Use Combined Antihypertensive Drugs? Free Combinations or Single Pill Combinations (SPCs)?

Recommendations

For hypertensive patients with BP ≥140/90 mmHg, a combination of antihypertensive drugs is initially recommended (1B).

For hypertensive patients requiring combination therapy, an SPC is recommended as priority (2C).

As an SPC, use of a renin–angiotensin system inhibitor (RASI) + CCB or RASI + diuretic combination is preferably recommended (2C).

Evidence and rationale

The combination of antihypertensive drugs is an important treatment strategy for patients with hypertension. The initial combination therapy can effectively control BP, reduce cardiovascular risk, and reduce adverse drug reactions. The results of a systematic review showed that, compared with high-dose CCB monotherapy, standard dose CCB + ARB combination therapy could effectively control BP (SBP: WMD = –2.52 mmHg, 95% CI: –3.76 mmHg to –1.28 mmHg; DBP: WMD = –2.07 mmHg, 95% CI: –3.73 mmHg to –0.42 mmHg),[190] and reduce the risk of adverse reactions (RR = 0.84, 95% CI: 0.74–0.95)[190] and the risk of MACEs (RR = 0.84, 95% CI: 0.76–0.93).[191]

As a new type of combined medication, an SPC typically comprises two or more antihypertensive drugs with different mechanisms of BP control. Compared with single-drug free-combination therapy, an SPC has the advantages of convenient use, good treatment compliance, and efficacy, and represents a new trend in combination therapy. The results of a systematic review showed that SPCs with different ingredients showed better treatment compliance (OR = 1.85, 95% CI: 1.37–2.49)[192] and medication persistence[193] than free combinations. For the selection of an SPC, the combination treatment scheme preferentially recommended by most hypertension guidelines is ARB or ACEI combined with CCB or diuretics, such as ACEI or ARB + dihydropyridine CCB, and ACEI or ARB + thiazide diuretics.[3] The results of a systematic review showed that the combination of ACEI/ARB and CCB fared better at improving the endocrine metabolism function and renal function of patients with hypertension than did other double or triple drug combinations.[194]

In clinical practice, the dosage should be more carefully considered in older or frail patients, and changes in their BP and patient tolerance should be monitored more closely when using combined antihypertensive drugs in this population. The risk of hypertension increases due to changes in the pharmacokinetics and pharmacodynamics of antihypertensive drugs and hypotension. Therefore, the strategy of an initial small-dose combination treatment should be adopted when necessary.[195] Clinicians should consider contraindications or possible adverse reactions to drug ingredients according to the specific conditions of the patients and should adopt an appropriate combined drug regimen. For instance, caution should be exercised in selecting SPCs containing thiazide diuretics in patients with hypertension who have gout and hyperuricemia.

Clinical Question 15: Choice of Medication in Patients with Hypertension and CHD

Recommendations

In hypertensive patients with CHD who manifest angina pectoris, β-blocker and CCB are recommended (1C).

In hypertensive patients with CHD and prior myocardial infarction, β-blocker and ACEI/ARB are recommended (1C).

Evidence and rationale

Antihypertensive medications (e.g., β-blockers, CCB, or ACEI/ARB) can alleviate myocardial ischemia and prevent serious cardiovascular events (e.g., death, myocardial infarction, or reinfarction) by improving the coronary blood supply and reducing myocardial oxygen consumption. However, drugs for patients with hypertension and

different types of CHD should be selected according to their specific conditions.[23] The recommendations on antihypertensive medication for patients with CHD are consistent with domestic and foreign guidelines.[3,6,134,196]

Beta-blockers and CCBs are recommended as first-choice medications for hypertensive patients with CHD who manifest with angina. The ACTION trial showed that CCB can reduce the risk of a composite of all-cause mortality, cardiovascular event, or procedure (HR = 0.89, 95% CI: 0.83–0.95) in patients with stable angina pectoris.[197] For patients with stable angina pectoris, no statistically significant difference in the total mortality was seen after treatment with a β-blocker (metoprolol) or a CCB (verapamil) (OR = 0.87, 95% CI: 0.48–1.56).[198] A systematic review showed that β-blockers and CCB were equivalent in the treatment of stable angina pectoris.[199]

For patients with hypertension and CHD who have a history of myocardial infarction, a β-blocker or ACEI/ARB is recommended as the first-line treatment option. A systematic review showed that compared with the placebo or no-intervention groups, β-blocker can reduce the risk of all-cause mortality (RR = 0.81, 95% CI: 0.73–0.90) and MACE (RR = 0.72, 95% CI: 0.62–0.83).[200] The Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) study showed that an ARB (telmisartan) was equivalent to an ACEI (ramipril) in terms of the effect of alleviating the risk of all-cause mortality (RR = 0.98, 95% CI: 0.90–1.07), cardiovascular mortality (RR = 1.00, 95% CI: 0.89–1.12), and myocardial infarction (RR = 1.07, 95% CI: 0.94–1.22).[201]

Individualized medication recommendations should be based on patient complications, drug tolerance, and contraindications. For example, beta-blockers should be discontinued in patients with severe bradycardia, high atrioventricular block, or asthma. Non-dihydropyridine CCB should be avoided in patients with HF, severe bradycardia, and atrioventricular block, because they inhibit cardiac conduction. ARBs can be used as an alternative in patients who cannot tolerate ACEIs.

Clinical Question 16: Recommendation of First-Line Antihypertensive Medications in Patients with Hypertension and HF

Recommendations

Angiotensin-receptor neprilysin inhibitor (ARNI) is recommended to replace ACEI/ARB as the first choice in patients with hypertension and HFrEF (2B).

ARNI/ARB/ACEI can be used as the first choice in patients with hypertension and HFpEF (2C).

Evidence and rational

ARNI is a novel drug used in the treatment of HFrEF to control BP and improve the prognosis of CVDs. The eutecticum of sacubitril and valsartan is a first-in-class representative drug that exerts its effects on diuresis, natriuresis, vasodilation, and aldosterone secretion inhibition through simultaneous renin–angiotensin–aldosterone system (RAAS) blockade and natriuretic peptide system activation.[202]

Instead of ACEIs/ARBs, ARNI is recommended as a first-line RASI to control BP in patients with hypertension and HFrEF. The results of a systematic review published in 2021 that included 10 studies of 1689 patients with chronic HF showed that the SBP and heart rate in the ARNI group were better controlled than those in the non-ARNI group (including ARBs and ACEIs), while DBP showed no significant difference. In terms of the safety consideration, the ARNI group had a lower risk of hyperkalemia and improved renal function in patients with renal insufficiency.[203] In addition, for hypertensive patients with HFrEF, the combination of a β-blocker, mineralocorticoid receptor antagonist (MRA) and sodium-glucose co-transporter 2 inhibitor (SGLT2i) is also the basic treatment, which can reduce BP and hospitalization rate of HF and improve prognosis.[204]

RASIs are recommended to control BP and improve the prognosis of CVD in patients with hypertension combined with HFpEF, particularly in those with hypertension-induced HF, whose BP levels remain higher despite symptoms of HF. The PARAMOUNT-HF study showed that N-terminal pro-B-type natriuretic peptide (NT-proBNP) was significantly reduced in the ARNI group as compared to in the valsartan group after 12 weeks of treatment in patients with HFpEF.[205] The Prospective Comparison of ARNI with ARB on Management of Heart Failure with Preserved Ejection Fraction (PARAGON-HF) study demonstrated that, compared with valsartan, ARNI did not significantly reduce the main composite endpoint of cardiovascular death or total HF hospitalization (first and recurrent) among patients with HFpEF. However, *post hoc* analysis showed that, in the 12 preset subgroups, sex and left ventricular ejection fraction (LVEF) had a higher effect on the risk of HF. The incidence of primary endpoint events decreased by 27% in the female subgroup, and by 22% in the LVEF ≤57% subgroup.[206,207] Herein, this current guideline recommends RASIs, which include ARNI/ARB/ACEI, and can be used as the first choice in patients with hypertension and HFpEF. In addition, considering that SGLT2i can significantly improve the prognosis of patients with HFpEF, and as MRA can improve diastolic function in patients with hypertension complicated with HFpEF, SGLT2i, and MRA are also recommended.[204]

ARNI has been shown to be safe and has a low incidence of severe adverse events, but further large-sample-size clinical trials are needed to investigate its long-term efficacy and safety in hypertensive patients with chronic HF.

Clinical Question 17: Choice of Medications in Hypertensive Patients with a History of Stroke or Transient Ischemic Attack (TIA)

Recommendations

For hypertensive patients with a history of stroke or TIA, ACEI (1A), diuretic (1A), or ACEI plus diuretic (1A) are

recommended. CCB (2C) or ARB (2C) may be considered if these agents are inappropriate or ineffective.

For hypertensive patients with a history of stroke or TIA, β-blockers are not recommended as first-line antihypertensive agents (1A).

Evidence and rationale

Hypertension is a major risk factor for stroke. Poorly controlled BP significantly increases the risk of stroke recurrence and antihypertensive medications can significantly reduce the risk of stroke recurrence and all-cause mortality.[208–210] An existing systematic review[211] showed that, compared with the placebo or no treatment, ACEI (RR = 0.73, 95% CI: 0.64–0.84) and diuretic (RR = 0.72, 95% CI: 0.59–0.87) interventions significantly reduced the risk of stroke recurrence in patients with a history of stroke or TIA. However, ARB (RR = 0.95, 95% CI: 0.87–1.03) and β-blockers (RR = 0.94, 95% CI: 0.75–1.18) had no significant effect. A network meta-analysis showed that compared with placebo, ACEI in combination with diuretics reduced the risk of stroke recurrence (OR = 0.54, 95% CI: 0.33–0.90).[212] Currently, the efficacy of CCB in reducing the risk of recurrent stroke in patients with a history of stroke remains controversial. A recent systematic review showed that, compared with non-CCB antihypertensive regimens, CCB monotherapy reduced the risk of stroke recurrence (OR = 0.41, 95% CI: 0.24–0.70).[213] However, another systematic review showed that CCB intervention did not significantly reduce the risk of recurrent stroke as compared to placebo or no treatment (RR = 0.55, 95% CI: 0.18–1.67).[211] Although current evidence suggests that ARBs do not significantly reduce stroke recurrence, they can be considered for patients with a history of stroke or TIA who are intolerant to ACEI. In addition, despite conflicting evidence on the effectiveness of CCB in reducing stroke recurrence, CCB can be considered for patients who are intolerant or contraindicated to the above-recommended regimens, given their widespread use in China and well-documented use in primary stroke prevention.

Owing to the high risk of cardiovascular events in patients with hypertension with a history of stroke or TIA, physicians should carefully assess the BP status of these patients, adjust medications gradually, and monitor them closely for serious adverse drug reactions.

Clinical Question 18: What Drugs are Recommended to Improve the Prognosis of Patients with Hypertension and Type 2 Diabetes?

Recommendations

In patients with hypertension and type 2 diabetes, ACEI/ARB is recommended for BP control (1B).

In patients with hypertension and type 2 diabetes, SGLT2i (2B) or GLP-1RA (2B) is recommended for optimal treatment.

Evidence and rationale

For patients with hypertension and diabetes, failure to control BP and glucose may lead to complications such as myocardial infarction, stroke, CKD, peripheral neuropathy, and retinopathy. Besides lifestyle intervention, rational drug therapy is essential to improve the long-term prognosis of these patients. A systematic review has shown that in patients with hypertension and type 2 diabetes, ACEI/ARB reduced the risk of MACE (RR = 0.78, 95% CI: 0.66–0.91) and HF (RR = 0.72, 95% CI: 0.61–0.83) compared with CCB. Additionally, ACEI/ARB decreased the risk of main composite endpoint events (RR = 0.76, 95% CI: 0.58–0.98), HF (RR = 0.59, 95% CI: 0.38–0.92), cardiovascular mortality (RR = 0.63, 95% CI: 0.42–0.95), and all-cause mortality (RR = 0.61, 95% CI: 0.45–0.84) compared with β-blockers.[214]

SGLT2i, a new oral hypoglycemic drug, reduces the reabsorption of glucose and sodium in the kidneys by inhibiting sodium-glucose cotransporter-2, thereby lowering glucose and BP.[215] GLP-1RA is a non-insulin injectable hypoglycemic drug that lowers glucose, promotes weight loss, and improves blood lipids by activating the glucagon-like peptide-1 receptor.[216] Compared with placebo, SGLT2i reduced the risk of MACE (HR = 0.90, 95% CI: 0.85–0.95), cardiovascular mortality (HR = 0.85, 95% CI: 0.78–0.93), HF admissions (HR = 0.68, 95% CI: 0.61–0.76), and CKD progression (HR = 0.62, 95% CI: 0.56–0.70), as confirmed by a systematic review.[217] A network meta-analysis showed that GLP-1RA reduced the risk of all-cause mortality, cardiovascular mortality, and non-fatal myocardial infarction in patients with type 2 diabetes.[218] Another systematic review also found that GLP-1RA reduced the risk of all-cause mortality (HR = 0.88, 95% CI: 0.83–0.95), cardiovascular mortality (HR = 0.88, 95% CI: 0.81–0.96), and myocardial infarction (HR = 0.91, 95% CI: 0.84–1.00).[219] Given the protective effects of SGLT2i and GLP-1RA on cardiovascular and renal function, and in line with recent recommendations in both domestic and international guidelines, our guideline recommends that patients with hypertension and type 2 diabetes be treated appropriately with SGLT2i or GLP-1RA.[38,142,143,146,220]

Clinically, the combination of ACEI and ARB is not recommended to lower BP due to the risk of hypotension, hyperkalemia, and renal deterioration.[201] Additionally, potential adverse effects such as urinary tract and reproductive tract infections with SGLT2i and gastrointestinal reactions with GLP-1RA should be monitored.[218]

Clinical Question 19: Are RASIs Recommended as First-Choice Antihypertensive Drugs in CKD Patients?

Recommendations

We recommend that a RASI be used in CKD patients with microalbuminuria and proteinuria (1B).

We suggest that a RASI may be used in CKD patients without microalbuminuria and proteinuria (2B).

Evidence and rationale

The goals of antihypertensive treatment in CKD patients are to lower BP and reduce CVD and mortality. A systematic review and meta-analysis revealed that in non-diabetic CKD with proteinuria, compared with placebo or active controls, RASI therapy with ACE inhibitors or angiotensin II receptor blockers significantly reduced the risk of composite renal failure events, including ESRD, a doubling of serum creatinine, and a 50% reduction in GFR (RR = 0.63, 95% CI: 0.52–0.75). However, in the proteinuria-negative subgroup, RASI showed no significant effect on renal failure risk (RR = 0.64, 95% CI: 0.18–2.30). For cardiovascular events, RASI was not associated with a significantly reduced risk in both proteinuria-positive and proteinuria-negative groups.[221] A systematic review in CKD patients with diabetes revealed that, compared to placebo or no treatment, ACEI significantly reduced the risk of ESRD and progression from micro- to macroalbuminuria (RR = 0.60, 95% CI: 0.39–0.93; RR = 0.45, 95% CI: 0.29–0.69) and significantly increased the chance of regression from micro- to normoalbuminuria (RR = 3.06, 95% CI: 1.76–5.35). The effect of ARB treatment on CKD patients with diabetes is similar to that of ACEI. Although there was no significant reduction in all-cause mortality in the ACEI or ARB group compared with placebo or no treatment, a subgroup analysis showed a significant reduction in all-cause mortality with the maximum tolerable dose of ACEI (RR = 0.78, 95% CI: 0.61–0.98). However, there was no decrease in all-cause mortality in patients using half or less than half the maximum tolerable dose of ACEI.[222]

In CKD patients with significantly reduced renal function, RASI may increase the risk of hypotension, hyperkalemia, or decreased renal function. For RASI, it is recommended to start at a low dose, monitor renal function, potassium, and BP, and gradually titrate to the maximum tolerable dose. If potassium levels in the blood exceed 5.5 mmol/L, estimated glomerular filtration rate (eGFR) decreases by 25% or more, or serum creatinine increases by 30% or more after starting RASI treatment, other causes of kidney deterioration, such as volume depletion or concurrent medication, should be ruled out, and RASI dose reduction or discontinuation should be considered.

Clinical Question 20: Which Hypertensive Patients should Take Aspirin?

Recommendations

For hypertensive patients with CHD, ischemic stroke, or peripheral vascular disease, it is recommended to take 75–100 mg/day of aspirin for long-term secondary prevention (1A).

For those aged 40–65 years with hypertension and cardiovascular risk, if the risk of bleeding is not high, low-dose aspirin (75–100 mg/day) can be considered for primary prevention (2B).

For high-risk groups for bleeding (e.g., history of gastrointestinal bleeding, recent cerebral hemorrhage, use of drugs that increase bleeding risk, uncontrolled hypertension), aspirin for primary prevention is not recommended (2C).

Evidence and rationale

The primary cause of acute cardiovascular events in patients with ASCVD is thromboembolism from ruptured atherosclerotic plaques. Aspirin has an antiplatelet aggregation effect that reduces thrombosis and prevents cardiovascular events.[223,224] However, aspirin increases the risk of bleeding, particularly gastrointestinal bleeding, so its benefit–risk ratio must be carefully evaluated in clinical practice.[225]

For secondary prevention of ASCVD patients, both domestic and international guidelines recommend that hypertensive patients with ischemic heart disease use low-dose aspirin for long-term secondary prevention.[5,75,226] However, for hypertensive patients without ASCVD, aspirin use for primary prevention varies internationally. The ESC/ESH hypertension guideline in 2018 clearly states that aspirin is not recommended for primary prevention in hypertensive patients.[5] Several guidelines and expert consensus suggest low-dose aspirin (75–150 mg/day) may be considered for primary prevention in high-risk groups such as patients with hypertension and diabetes, CKD, or cardiovascular risk aged 50–69 years (10-year cardiovascular risk ≥10% or hypertension with ≥3 other risk factors).[146,227,228] According to A Study of Cardiovascular Events in Diabetes (ASCEND) study, compared with placebo, aspirin treatment has a lower incidence of severe vascular events but a higher incidence of major bleeding in adult diabetic patients without evident CVD.[229] Primary prevention with aspirin has shown significant risk reductions for MACE (HR = 0.89, 95% CI: 0.84–0.95) and myocardial infarction (HR = 0.85, 95% CI: 0.76–0.87).[230] However, it increases risks of major hemorrhage (HR = 1.43, 95% CI: 1.30–1.56), intracranial hemorrhage (HR = 1.34, 95% CI: 1.14–1.57), and gastrointestinal bleeding (HR = 1.56, 95% CI: 1.38–1.78).

In 2022, Calderone *et al*[231] published the largest meta-analysis on the efficacy of aspirin in primary prevention, which included 21 RCTs involving 173,810 patients without CVD. The results showed that aspirin could reduce the risk of MACE by 11%, but it also increased the risk of major hemorrhage and gastrointestinal bleeding, particularly in individuals under 65 years old. The ACC/AHA Guidelines for Primary Prevention of Cardiovascular Diseases in 2019,[75] the Guidelines for Primary Prevention of Cardiovascular Diseases in China in 2020,[32] and the Guidelines of the United States Preventive Services Working Group in 2022[232] all recommend an age limit of 40 years for primary prevention with aspirin.

Furthermore, several guidelines and expert consensus indicate that aspirin is not recommended for primary prevention in the following groups: individuals aged ≥60 years; those with a high risk of bleeding (e.g., those taking antiplatelet drugs, anticoagulants, glucocorticoids, or non-steroidal anti-inflammatory drugs that increase bleeding risk, as well as those with a history of gastrointestinal bleeding, peptic ulcer, cerebral hemorrhage within the

last 3 months, thrombocytopenia, coagulation disorders, severe liver disease, CKD stages 4–5, non-eradicated *Helicobacter pylori* infection, or uncontrolled hypertension). In these cases, the risk of bleeding is assessed to be greater than the benefit of thrombosis prevention.[227,228,232]

In conclusion, the benefits and risks of aspirin for primary prevention in hypertension patients without ASCVD should be carefully evaluated, and the recommended therapy should be tailored to the individual patient's situation.

Clinical Question 21: What is the Follow-Up Interval after Pharmacological Intervention Initiation in Hypertensive Patients?

Recommendations

We recommend following up hypertensive patients within 2–4 weeks after the initiation or adjustment of antihypertensive medication until the BP target is reached (GPS).

We recommend following up hypertensive patients at three-month intervals after reaching the BP target (GPS).

Evidence and rationale

BP control can reduce the occurrence of cardiac, cerebral, renal, vascular, and other complications. Therefore, follow-up visits after the initiation of pharmacological intervention in hypertension are significant. After a systematic review of this issue, no systematic reviews/meta-analyses or original studies were included. The recommendations are thus based on expert consensus and previous guidelines.

Current domestic and international guidelines recommend the same approach. The 2017 ACC/AHA Guidelines on hypertension recommend monthly follow-up for medication adherence/compliance and effect after the initiation or adjustment of pharmacological interventions in hypertensive adults until reaching the BP target.[6] The 2020 International Society of Hypertension Global Hypertension Practice Guidelines recommend monthly follow-up after antihypertensive medication initiation for hypertensive patients.[30] Similar follow-up intervals are recommended in the Clinical Practice Guideline for Adult Hypertension—Prevention, Screening, Counseling and Management in the United States (2018)[138] and the 2021 World Health Organization Guideline for the pharmacological treatment of hypertension in adults. After reaching the BP target, follow-up every 3–6 months is recommended.[4]

Collectively, clinical adjustments in follow-up intervals and the scope of follow-ups for hypertension patients should be tailored to the treatment approach and individual patient conditions.

Clinical Question 22: How to Manage Hypertension Patients in the Community?

Recommendations

Multifaceted management models involving community and village doctors are recommended (1A).

Evidence and rationale

The prevalence of hypertension is increasing worldwide, and maintaining the effects of antihypertensive treatment in community-based management is essential. The 2023 ESH Hypertension Guideline suggests that alternative models of hypertension care, in which other health professionals participate, may also be tested and implemented.[3] The 2017 ACC/AHA Hypertension Guideline suggests that team-based care for hypertension should include the patient, the patient's primary care provider, and other professionals such as cardiologists, nurses, pharmacists, physician assistants, dietitians, social workers, and community health workers.[6] In China, exploratory studies on community hypertension management, like the Shougang study and the Kailuan study, were conducted in the last century. This century has seen urban community hypertension management studies, such as the Shanghai Minhang community study, the Hangzhou community study, and the Fuwai Wang Zengwu team's community hypertension study. Evidence from these studies supports the community as key to hypertension management in urban areas, though there is a lack of evidence-based medical research on rural community management models. Recently, the China Rural Hypertension Control Program (CRHCP) study tested the effectiveness and safety of intensified antihypertensive strategies led by village doctors, along with multifaceted management models, in community-based hypertensive patients. In this study, 326 villages were assigned (1:1) to either the intervention group (village doctor-led multifaceted intervention) or the control group (enhanced usual care). The intervention group employed multifaceted interventions: village doctors were given primary responsibility and supported by a three-level management system (county–village–hamlet). Simulated social security support, including drug discounts and price reductions, improved drug accessibility. Village doctors were trained to use simplified drug regimens, implement information management systems, and promote an innovative intensified antihypertensive target of 130/80 mmHg. Patient-level interventions included health education and home self-testing of BP. After 36 months, it was found that multifaceted management models led by village doctors could achieve the intensified antihypertensive goal of 130/80 mmHg and effectively reduce CVD and mortality.[125,126] This confirmed that intensified BP interventions and multifaceted management models led by village doctors were feasible, safe, and effective in reducing CVD and mortality.

Clinical Question 23: Should Spironolactone be the Fourth-Line Medication for Patients with Resistant Hypertension?

Recommendations

A low dose of spironolactone (20–40 mg/day) is recommended as the fourth-line medication for patients with resistant hypertension whose serum potassium is <4.5 mmol/L and eGFR is ≥45 mL·min^{-1}·1.73 m^{-2} (1B).

Evidence and rationale

Resistant hypertension is a complex condition with challenging treatment needs and a higher likelihood of target

organ damage. Although there is no consensus on the definition of resistant hypertension, our guideline defines it as BP (including HBPM or ABPM) that fails to reach the target level in patients treated for at least 4 weeks with three antihypertensive medications (including a CCB, ACEI/ARB, and thiazide-type diuretic) at optimal or maximally tolerated doses.[3]

Multiple guidelines recommend spironolactone as the fourth-line antihypertensive medication for resistant hypertensive patients whose serum potassium is <4.5 mmol/L and eGFR is ≥45 mL·min^{-1}·1.73 m^{-2}.[30,76] A meta-analysis indicated that additional spironolactone significantly reduced office SBP (WMD = −13.15 mmHg, 95% CI: −20.79 mmHg to −5.51 mmHg), office DBP (WMD = −3.54 mmHg, 95% CI: −5.92 mmHg to −1.16 mmHg), 24-h average SBP (WMD = −8.71 mmHg, 95% CI: −11.46 mmHg to −5.95 mmHg), and 24-h average DBP (WMD = −4.27 mmHg, 95% CI: −6.2 mmHg to −2.34 mmHg) compared to placebo or other antihypertensive medications.[233] Given the side effects of spironolactone, patients' electrolyte levels and renal function should be monitored during administration. Multiple guidelines recommend spironolactone at 25–50 mg/day for antihypertensive treatment, based on the Prevention and Treatment of Hypertension with Algorithm-based therapy (PATHWAY) 2 study.[3,30,76] Considering the production standard of spironolactone in our country, a dosage of 20–40 mg/day is recommended as the fourth-line drug for resistant hypertension treatment.

Clinical Question 24: For Whom is Renal Denervation (RDN) Suitable?

Recommendations

RDN can be used as a BP-lowering strategy in hypertensive patients with resistant hypertension, intolerance to antihypertensive therapy, and clinical features consistent with sympathetic hyperactivity (2B).

Evidence and rationale

BP control remains a challenge in some patients with resistant hypertension, for whom antihypertensive drugs alone may not achieve the target BP. Device-based therapies provide a reasonable alternative. Recent clinical research on RDN has shown promising progress.[234] Since 2017, randomized, sham-controlled studies like SPYRAL HTN-OFF MED,[235] SPYRAL HTN-ON MED,[236] the Global SYMPLICITY Registry,[237] and the three-year follow-up results of SPYRAL HTN-ON MED[238] have provided increasing evidence for the long-term efficacy and safety of RDN. Guidelines and consensus statements from Asia and Europe indicate that RDN may be a safe and effective treatment for patients with resistant hypertension or mild to moderate hypertension,[3,5,46,239] with a low incidence of procedure-related complications and a favorable safety profile.

A systematic review of six RCTs showed that RDN significantly reduced office blood pressure monitoring (OBPM) (SBP: WMD = −5.10 mmHg, 95% CI: −7.31 mmHg to −2.90 mmHg; DBP: WMD = −3.11 mmHg, 95% CI: −4.43 mmHg to −1.78 mmHg) and 24-h ABPM (mean SBP: WMD = −3.52 mmHg, 95% CI: −4.94 mmHg to −2.09 mmHg; mean DBP: WMD = −1.93 mmHg, 95% CI: −3.04 mmHg to −0.83 mmHg)[240] compared with a sham control. Another systematic review published in 2022 showed that RDN significantly reduced OBPM (SBP: WMD = −8.2 mmHg, 95% CI: −17.1 mmHg to −0.8 mmHg) and 24-h ABPM (mean SBP: WMD = −10.0 mmHg, 95% CI: −16.6 mmHg to −3.3 mmHg) compared with sham control.[238] Compared with first-generation RDN technology,[241] the second-generation RDN technology further improved BP-lowering efficacy, with the average ABPM daytime SBP reduction being significantly greater (6.12 mmHg *vs*. 2.14 mmHg, interactive *P*-value = 0.04). However, there is currently no direct evidence that RDN reduces cardiovascular events.

Drug treatment remains the preferred method for most hypertensive patients, but some experience issues like drug intolerance or poor compliance. A European survey showed that approximately one-third of hypertensive patients prefer RDN treatment.[242] Therefore, RDN may be considered as a BP-lowering strategy in hypertensive patients who cannot tolerate pharmacotherapy (e.g., due to allergies or adverse reactions), whose clinical features are consistent with sympathetic hyperactivity, and who are willing to consider device therapy.

Clinical Question 25: Principles of Initial Management of Hypertensive Emergencies

Recommendations

Patients with significantly elevated BP (SBP >180 mmHg and/or DBP >120 mmHg) should be evaluated as soon as possible for evidence of new or worsening target organ damage (GPS).

Patients with evidence of new and progressively worsening target organ damage should be admitted to the emergency resuscitation unit or an intensive care unit for continuous monitoring of BP and target organ damage and for parenteral administration of an appropriate agent (GPS).

The principles of BP management in hypertensive emergencies: It is recommended to lower BP to a relatively safe range while ensuring adequate organ perfusion (SBP should be reduced by no more than 25% within the first hour; then, if stable, to 160/100 mmHg within the next 2–6 h; and then cautiously to the target level during the following 24–48 h). The magnitude and rate of BP reduction should be individualized and adjusted according to the patient's specific situation (GPS).

For patients with severe comorbidities (e.g., severe preeclampsia or eclampsia, pheochromocytoma crisis), SBP should be reduced to less than 140 mmHg within the first hour of treatment (GPS).

For patients with aortic dissection, SBP should be reduced to 110–120 mmHg during the first hour of treatment while controlling heart rate to <60 bpm, if tolerated (GPS).

Evidence and rationale

Acute HMOD is the core feature of hypertensive emergencies and the critical factor in prognosis.[3,6,243–245] At present, no specific evidence was retrieved, so recommendations are based on existing guidelines and expert consensus.

For the initial management of patients with hypertensive emergencies, previous guidelines and consensus recommendations are relatively consistent, advising that target organ impairment should be assessed as soon as possible for rapid identification of patients with hypertensive emergencies. For identified patients, antihypertensive therapy and continuous monitoring should be initiated immediately.[3,6,243,244] For the rate and magnitude of antihypertensive therapy in patients with hypertensive emergencies, the 2017 ACC/AHA guidelines recommend that for adults without a compelling condition, SBP should be reduced by no more than 25% within the first hour; then, if stable, to 160/100 mmHg within the next 2–6 h; and then cautiously to normal during the following 24–48 h.[6] Other international guidelines and consensus documents emphasize individualized treatment strategies while ensuring organ perfusion. The magnitude and rate of BP reduction depend on the type of hypertensive organ damage and the patient's condition.[3,6,243,244] Regarding the treatment strategy for patients with hypertensive emergencies and severe comorbidities, the 2017 ACC/AHA guidelines recommend that for adults with a compelling condition (e.g., aortic dissection, severe preeclampsia or eclampsia, or pheochromocytoma crisis), SBP should be reduced to less than 140 mmHg during the first hour.[6] The 2023 ESC/ESH guideline[5] and 2020 ISH guideline[243] are consistent in recommending that mean arterial pressure (MAP) should be reduced by 20–25% within hours in patients with hypertensive emergencies with or without acute renal failure, by 20–25% immediately in hypertensive encephalopathy; and SBP should be immediately reduced to <140 mmHg in patients with an acute coronary event or acute cardiogenic pulmonary edema; patients with eclampsia and severe pre-eclampsia/hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome should immediately reduce SBP to <160 mmHg and DBP to <105 mmHg. For patients with acute aortic dissection, the 2017 ACC/AHA guideline recommends that SBP should be reduced to less than 110–120 mmHg within 1 h[6]; other guidelines recommend that SBP should be reduced to <120 mmHg immediately while controlling heart rate to <60 bpm.[5,243,246–248] The primary goal of these recommendations is to reduce shear stress on the diseased segment of the aorta by reducing BP and cardiac contractility, though there is limited evidence to support this.

Clinical Question 26: Which Types of Hypertensive Patients Need to be Screened for Secondary Hypertension?

Recommendations

The following patients are recommended to be screened for common secondary hypertension (2C): (1) newly diagnosed hypertensive patients; (2) patients with hypertension onset at <40 years; (3) patients with resistant hypertension; (4) hypertensive patients with clinical clues of secondary hypertension or extensive hypertension-mediated target organ damage.

Evidence and rationale

Newly diagnosed hypertensive patients should be screened for common secondary hypertension causes, including obstructive sleep apnea (OSA), renovascular hypertension, primary aldosteronism (PA), renal parenchymal disease, and others. Screening for secondary hypertension should also be performed in patients with onset of hypertension at <40 years, especially those with BP levels higher than 160/100 mmHg. Delayed diagnosis of secondary hypertension can further aggravate target organ damage beyond the effects of long-standing hypertension.[246]

Patients with resistant hypertension are at higher risk of target organ damage and MACE, including carotid intima-media thickening, fundus lesions, left ventricular hypertrophy and HF, myocardial infarction, stroke, renal dysfunction, and death. Resistant hypertension also imposes considerable public health, economic, and social burdens due to treatment costs, related disability, and premature death.[249,250] Even if BP is controlled, patients with resistant hypertension have a higher risk of CVDs and all-cause mortality.[251] Screening for secondary hypertension in these patients, identifying the cause, and providing targeted treatment can reduce the risk of cardiovascular and cerebrovascular events.

Hypertensive patients with clinical indications or extensive HMOD should be screened for secondary hypertension.[3] Patients with secondary hypertension often present characteristic clinical manifestations and signs related to the primary disease, which can provide clues for screening. Common causes and related symptoms and signs of secondary hypertension are shown in Table 4.

Clinical Question 27: Who should be Screened for PA?

Recommendations

We recommend screening for PA in all patients with hypertension, especially in those with newly diagnosed hypertension, resistant hypertension, or hypokalemia (2C).

Evidence and rationale

PA, which accounts for 5–10% of hypertensive patients,[252] is one of the most common secondary causes of hypertension. Compared with essential hypertension (EH), patients with PA have an increased risk of cardiovascular events and mortality.[253,254] Early screening, timely diagnosis, and treatment significantly improve the prognosis for patients with PA. However, recommendations vary regarding which patients should be screened for PA. European and American guidelines recommend screening high-risk patients (e.g., those with hypokalemia, resistant hypertension), while the Japanese guideline recommends that all hypertensive patients be screened for PA.[255–257]

Table 4: Common causes and suggestive findings of secondary hypertension.

Causes	Suggestive findings
OSA	Snoring, obesity (also can be present in non-obese), morning headache, daytime somnolence, nocturnal hypertension
Renal parenchymal disease	A history of kidney disease, hematuria, proteinuria, nocturia, renal dysfunction, anemia, abnormal size and morphology of kidney
Renovascular disease	Recurrent flash pulmonary edema, abdominal vascular bruit, unilateral atrophic kidney, hypokalemia, resistant hypertension, significantly elevated serum creatinine after the administration of RASI
PA	Hypokalemia, adrenal incidentaloma, muscle weakness (rare), AF of unknown origin
Pheochromocytoma/ paraganglioma	Paroxysmal, sustained hypertension or paroxysmally increasing hypertension, headache, perspiration, palpitations when attack, abnormal glucose or lipid metabolism, BP surges precipitated by drugs (e.g., beta-blockers, metoclopramide, sympathomimetics, opioids, and monoamine oxidase inhibitor)
Cushing's syndrome	Moon face, central obesity, sanguineous temperament, skin striae, abnormal glucose metabolism, hypokalemia, and osteoporosis
Thyroid disease	Hyperthyroidism: heat intolerance, hyperhidrosis, tachycardia, weight loss, diarrhea
	Hypothyroidism: cold intolerance, hypohidrosis, bradykinesia, bradycardia, weight gain, astriction
Aorta coarctation	Differences in BP ≥20 mmHg between upper-lower extremities, BP of lower extremities significantly lower than upper extremities (ABI <0.9), interscapular vascular bruit, rib notching on chest X-ray

1 mmHg = 0.133 kPa. ABI: Ankle-brachial index; AF: Atrial fibrillation; RASI: Renin–angiotensin system inhibitor; BP: Blood pressure; OSA: Obstructive sleep apnea; PA: Primary aldosteronism.

Real-world data indicate that the rate of screening for PA is extremely low, and many patients with PA may be missed if only high-risk patients are screened.[258–260] Screening for PA in all hypertensive patients will likely improve screening rates, reduce missed diagnoses, and improve long-term outcomes. Cost-effectiveness analyses show that screening for PA in all hypertensive patients not only saves medical costs but also offers health benefits, including fewer cardiovascular events and better BP control.[261,262] Notably, the prevalence of PA has been reported to be 4–7% among newly diagnosed hypertensive patients, and the rate of complete clinical success in PA patients who received surgery is up to 86%, suggesting that early screening in newly diagnosed hypertensive patients can significantly improve outcomes.[263] Additionally, in newly diagnosed hypertensive patients who have not yet commenced treatment, aldosterone and renin levels are unaffected by antihypertensive medications. Therefore, all newly diagnosed hypertensive patients should be screened for PA. Individuals with resistant hypertension or comorbid hypokalemia should also be screened, as PA is highly prevalent in these populations.[264–267]

Clinical Question 28: How to Screen for PA and Which Cutoff Value should be Recommended?

Recommendations

For PA screening, we recommend the plasma aldosterone-to-renin ratio (ARR) after patients remain in a non-recumbent position for at least 2 h (1B) as the cutoff.

We recommend an ARR of 2.0 ng·dL^{-1}/mU·L^{-1} as the cutoff if ARR is calculated by plasma aldosterone concentration (PAC)/plasma renin concentration (PRC), and 30 ng·dL^{-1}/ng·mL^{-1}·h^{-1} as the cutoff if ARR is calculated by PAC/plasma renin activity (PRA) (2C).

Evidence and rationale

The plasma ARR is the most commonly used screening test for PA. We recommend ARR as a screening test because it is widely available and demonstrates high sensitivity at the appropriate thresholds.

We suggest drawing blood after the patient has been in a non-recumbent position (sitting, standing, or walking) for at least 2 h to calculate the ratio of PAC to renin concentration (or renin activity). Common assays for measuring plasma aldosterone and renin include chemiluminescence and radioimmunoassay. Studies report that PRC measured by these methods shows a high level of concordance and similar efficacy for PA screening.[268] The chemiluminescence method is more widely used in clinical practice because it is easier and faster.[269] Setting the cutoff for PAC/PRC at 2.0 ng·dL^{-1}/mU·L^{-1}, the sensitivity is 0.9 and specificity is 0.8,[270] while setting the cutoff for PAC/PRA at 30 ng·dL^{-1}/ng·mL^{-1}·h^{-1}, results in sensitivity and specificity above 0.9.[271] Additionally, patients with PA often have a PAC ≥8 ng/dL.[272]

ARR is influenced by factors such as age, posture, and medications.[255,256,273] Although guidelines recommend ARR for PA screening, specific cutoff values are not consistent due to differences in populations, laboratory assays, and downstream diagnostic tests. To improve sensitivity and reduce missed diagnoses, a relatively low cutoff is generally selected, while a higher cutoff may improve specificity and avoid unnecessary investigations. Each center should select cutoffs considering detection reagents, measuring methods, and accuracy. A study from China using liquid chromatography-tandem mass spectrometry (LC-MS/MS) as the gold standard for detecting PAC found variation in measurement accuracy among different methods.[274] Although LC-MS/MS is accurate, it is complex and has limited feasibility.

Clinical Question 29: How to Confirm the Diagnosis of PA in Individuals with a Positive ARR?

Recommendations

We suggest the captopril challenge test (CCT) or seated saline infusion test (SIT) as the confirmatory test for PA (2C).

Evidence and rationale

Patients with a positive ARR should undergo at least one confirmatory test. Both the CCT and SIT demonstrate high diagnostic accuracy.[275,276] Compared with SIT, CCT is safer and more feasible in an outpatient setting.[277,278] Although guidelines recommend CCT or SIT as the confirmatory test, the suggested cutoff values vary, potentially due to selection bias, varied comparators, and different populations. Studies show that PAC post-CCT ≥11 ng/dL[275,279,280] or PAC post-SIT ≥8 ng/dL[278] demonstrates high sensitivity and specificity for PA diagnosis. However, a small proportion of false negatives or positives may occur with any confirmatory test, so a comprehensive evaluation of the patient's clinical characteristics is essential.

Clinical Question 30: Is a Washout of Interfering Medications Necessary When Screening for PA?

Recommendations

We recommend screening for PA without stopping interfering medications, though PA screening results should be carefully interpreted if these medications cannot be discontinued (2D).

Evidence and rationale

Commonly used antihypertensive drugs (e.g., dihydropyridine calcium channel blockers, ACE inhibitors, angiotensin II receptor blockers, diuretics, and beta-blockers) can influence plasma aldosterone and renin concentrations, thus affecting ARR. Current guidelines vary on whether to discontinue or switch antihypertensive drugs when screening for PA. The American Endocrine Society guidelines recommend that drugs should be stopped or switched to agents with minimal impact on ARR, but PA screening results with interfering medications may still be clinically interpretable.[256] The European Society of Hypertension (ESH) recommends that it is unnecessary to discontinue or switch interfering medications before screening but suggests cautious interpretation of results. In some undetermined cases, discontinuing or switching medications that influence ARR may be necessary.[255] The Japan Hypertension Association also recommends PA screening ideally without interfering antihypertensive medications. Although ACEIs, ARBs, and other drugs can affect ARR, their impact on clinical significance is limited.[257]

Guidelines also note that a washout of interfering antihypertensive medications is cumbersome, costly, and may cause BP fluctuations. Studies show that patients asked to undergo a drug washout often have poor compliance, which can reduce screening rates in practice.[258,281,282] For patients at high risk of PA (e.g., those with stages 2–3 hypertension, drug-resistant hypertension, hypertension with spontaneous or diuretic-induced hypokalemia, hypertension with adrenal incidentaloma, hypertension with a family history of early onset hypertension or young-age cerebrovascular accident, and hypertensive first-degree relatives of PA patients), if initial PA screening is negative while on interfering medications, a drug washout (discontinuation or switch to non-dihydropyridine calcium channel blockers or alpha-blockers) is recommended for 2 weeks before repeat screening (4 weeks for patients taking diuretics, including spironolactone).

If PA screening occurs with interfering medications, results should be interpreted with consideration of the agent's effects. Studies indicate that antihypertensive drugs may influence plasma aldosterone and renin levels but do not significantly reduce the screening efficacy of ARR.[257,283] Recent studies suggest lowering the ARR threshold for PA screening to 0.7–1.0 (ng/dl)/(mU/L) when taking interfering antihypertensive drugs.[283,284] Clinically, if a positive ARR is obtained while on ACEI/ARBs/non-dihydropyridine CCB/potassium-wasting diuretics, it is likely valid, and confirmatory tests may proceed.[255] If a patient at high PA risk has a negative ARR, a repeat test should be done 2 weeks after drug washout. In patients on beta-blockers (which may cause false positives), those with a normal ARR do not need further testing, while those with an elevated ARR should have repeat measurement after a 2-week washout.[255] Potassium-sparing diuretics (such as spironolactone) significantly impact ARR and require a 4-week washout before ARR measurement.[255,256]

Clinical Question 31: Who should be Screened for Cushing's Syndrome?

Recommendations

We recommend screening for Cushing's syndrome among adult hypertensive patients with the following characteristics (2C): (1) features that best discriminate Cushing's syndrome: easy bruising, facial plethora, proximal muscle weakness, and purple striae. (2) Other common clinical features: menstrual abnormalities, acne, weight gain, and central obesity. (3) Refractory hypertension. (4) Unusual osteoporosis for age. (5) Adrenal incidentaloma. (6) Type 2 diabetic patients who need insulin treatment or are on two or more anti-hypertensive drugs.

Evidence and rationale

Patients with Cushing's syndrome can develop hypertension, but there is no consensus on which group of hypertensive patients should be screened. Clinical features that best discriminate Cushing's syndrome include easy bruising, facial plethora, proximal muscle weakness, and purple striae.[285] Other common clinical features include menstrual abnormalities (frequent in 67% of Cushing's syndrome patients), acne (47%), weight gain (69%), and

central obesity (59%).[286] The annual incidence rate of Cushing's syndrome in the general population is only 2–3 per million.[287] However, up to 80% of patients with Cushing's syndrome develop secondary hypertension,[286] and as many as 8% of patients with refractory hypertension have hypercortisolemia.[287] Among patients with unusual osteoporosis for their age–which refers to males with normal sex hormones and females before menopause–[285,288] and people with adrenal incidentaloma,[285,289] the prevalence of Cushing's syndrome is significantly higher than that in the general population. Hyperglycemia and hypertension are clinical characteristics of excessive cortisol secretion. It has been reported that type 2 diabetic patients who need insulin treatment or are on two or more antihypertensive drugs have a higher prevalence of hypercortisolism than other type 2 diabetes patients (OR = 4.50, 95% CI: 1.51–13.62).[290] In this guideline, we recommend screening type 2 diabetic patients who need insulin treatment or are on two or more antihypertensive drugs, especially those with clinical features of central obesity, purple striae, etc.

Clinical Question 32: How to Screen for Cushing's Syndrome among Adult Hypertensive Patients?

Recommendations

For initial screening, we recommend one of the following tests for patients clinically suspected of Cushing's syndrome: (1) 1-mg overnight dexamethasone suppression test (2D). (2) 24-h urinary free cortisol (2C). (3) Late-night salivary cortisol (2C).

Evidence and rationale

A recently published international consensus on diagnosing and managing Cushing's syndrome recommended screening tests, including 24-h urinary free cortisol, late-night salivary cortisol, and the dexamethasone suppression test.[291] A meta-analysis comparing these initial screening tests showed that the sensitivity and specificity of late-night salivary cortisol, the overnight 1-mg dexamethasone suppression test, 24-h urinary free cortisol, and the low-dose 2-day dexamethasone test were 95.8%, 98.6%, 94.0%, and 95.3%, respectively, and 93.4%, 90.6%, 93.0%, and 92.8%, respectively.[292] The sensitivity of the overnight 1-mg dexamethasone suppression test was the highest, and the specificity of late-night salivary cortisol was the highest.

The screening value of each test may be affected by special circumstances. The collection time for saliva cortisol samples at night is 11–12 pm, which is unsuitable for those with abnormal circadian rhythms.[291] Currently, late-night salivary cortisol tests are not routinely performed in China. Urinary-free cortisol and late-night salivary cortisol are recommended to be tested twice or more.[285,291] The cutoff point for the overnight 1-mg dexamethasone suppression test is 50 nmol/L (1.8 μg/dL) cortisol concentration in plasma at 8 am. However, certain conditions can decrease dexamethasone absorption or accelerate its clearance, leading to false positives. Vomiting or diarrhea significantly shortens the gut transit time of dexamethasone. Concomitant treatment with CYP3A4 inducers (e.g., rifampicin, phenobarbital, and carbamazepine) accelerates dexamethasone metabolism. Increased glucocorticoid-binding globulin, induced by oral estrogen, pregnancy, or chronic active hepatitis, increases plasma cortisol concentrations. False negatives may occur from the simultaneous use of drugs that inhibit dexamethasone metabolism, such as cimetidine, diltiazem, and fluoxetine. Reduced serum albumin or glucocorticoid-binding globulin decreases plasma cortisol concentration.[291] To avoid screening test errors, it is recommended to use other screening tests, such as late-night salivary cortisol and 24-h urinary free cortisol, and to simultaneously detect serum dexamethasone concentration.[292] Clinicians can choose appropriate screening tests based on their suitability for a given patient. Patients with positive initial screening and suspected Cushing's syndrome should consult the endocrinology department for further evaluation.

Clinical Question 33: Which Hypertensive Patients should be Screened for Pheochromocytoma and Paraganglioma (PPGL)?

Recommendations

The following patients should be considered for PPGL screening: (1) Patients with paroxysmal hypertension and triad symptoms (headaches, palpitations, and sweating) (1C). (2) Patients with symptoms of PPGL triggered by adrenergic drugs, changes in abdominal pressure, anesthesia, or surgery (1C). (3) Patients with an incidentally discovered adrenal mass (1C). (4) Patients with a predisposition to hereditary causes (1C). (5) Patients with myocardial damage of unknown causes and stress-induced cardiomyopathy (2D).

Evidence and rationale

The main clinical manifestation of PPGL is elevated BP caused by catecholamine (CA) excess, which can cause complications and metabolic changes in target organs such as the heart, brain, and kidneys. The classical clinical presentation is hypertension (90–100%), which may be paroxysmal (40–50%), persistent (50–60%), or paroxysmal aggravation (50%) based on persistent hypertension. About 70% of patients can have OH in addition to hypertension. Most patients have resistant hypertension, and a few have normal BP.[6,30,46,47,293,294]

Due to differences in tumor location, continuous or paroxysmal secretion of adrenaline, norepinephrine, and dopamine, and varying involvement of adrenergic receptor subtypes, PPGL presents various clinical manifestations. Headache, palpitations, and excessive truncal sweating are the most common triad symptoms (40–48%) in PPGL patients with hypertension.[6,30,46,47,293,294] If patients present with hypertension, OH, and triad symptoms, the specificity of PPGL diagnosis is 95%.[293] The use of adrenergic drugs (e.g., dopamine receptor antagonists, sympathomimetics, opioids, norepinephrine or 5-hydroxytryptamine reuptake inhibitors, monoamine oxidase inhibitors), changes in abdominal pressure (e.g.,

pressing the abdomen or after urination), anesthesia, or surgical stress can trigger elevated BP and PPGL symptoms due to adrenergic receptor overstimulation, which is also significant in diagnosing PPGL.[47,293] Furthermore, an incidentally discovered adrenal mass, a family history of PPGL or PPGL-related inherited syndromes, and a previous history of PPGL are closely related to diagnosis, treatment, and prognosis, warranting screening.[6,30,46,47,293–295]

Myocardial damage in patients with PPGL is also a concern. CA-induced cardiomyopathy associated with PPGL includes arrhythmias, Takotsubo-like cardiomyopathy, angina pectoris, acute coronary ischemia, or even myocardial infarction and hypotensive shock. Autopsies found CA-induced cardiomyopathy in 58% of PPGL patients. In addition to ventricular hypertrophy from long-term severe hypertension, hypercatecholaminemia can lead to myocardial injury, fibrosis, and ischemia.[293,296,297] A cohort study showed a high incidence of chest distress and typical triad symptoms in PPGL patients with cardiac involvement, and larger tumors were more likely to present with hemorrhage or necrosis.[298] CA-induced cardiomyopathy may be considered if patients with PPGL have symptoms such as chest pain or HF and if electrocardiogram (ECG) indicates T-wave is low or inverted for three or more leads, abnormal ST segment or arrhythmia, echocardiography shows myocardial hypertrophy or left ventricular diastolic function reduction, reduced LVEF, abnormal ventricular wall motion and the improvement and disappearance of the above symptoms and signs after PPGL tumor resection.[293,296,297]

Clinical Question 34: How to Screen for PPGL?

Recommendations

We recommend plasma-free or urinary fractionated metanephrine (MN) and normetanephrine (NMN) as the first choice for biochemical testing of PPGL (1B).

Evidence and rationale

The measurements of plasma-free or urinary fractionated CA and metabolites of CA are the principal qualitative diagnostic evidence of PPGL. The prototype products of CA include dopamine, norepinephrine, and adrenaline. The intermediate metabolites include MNs (including NMN and MN), 3-methoxytyramine, and the main end-metabolites, including vanillylmandelic acid (VMA) and homovanillic acid (HVA).[293] MNs are intermediate metabolites of noradrenaline and adrenaline, which are continuously produced within adrenal medulla chromaffin cells and PPGL tumors and then leak into the circulation. Compared with CA, MNs maintain a higher concentration level, have a longer half-life, and are more stable. Their higher specificity and sensitivity can reflect the functional status of PPGL tumors, making them the preferred and recommended specific markers for PPGL.[6,30,46,47,293,294]

The sensitivity and specificity of plasma-free or urinary fractionated CA and its various products differ in the qualitative diagnosis of PPGL, among which MNs have higher sensitivity and specificity than CA prototypes and VMA. The detection of plasma-free or urinary MNs has a high sensitivity in the diagnosis of PPGL, but the false-positive rate is 19–21%.[293,294,299,300] The results of a systematic review showed that plasma-free MN combined with NMN had a higher diagnostic rate for PPGL than either MN or NMN measurement alone.[301] The sensitivity and specificity of plasma-free MNs are better than those of urinary MNs, and the false-positive rate of plasma-free MNs in the supine position is lower than in the sitting position.[293,294,299,300] The false-positive rate will be reduced when NMN or MN alone increases three-fold or more, or both increase, but further clinical examination should be carried out to confirm the diagnosis. For patients with mildly elevated MNs, the assay should be repeated to confirm after excluding influencing factors.[293] Simultaneous detection of plasma-free and 24-h urinary CA and MNs levels has high sensitivity and specificity, which can indicate PPGL diagnosis when it is 1.5–2.0 times higher than the upper limit of the normal reference value. With simultaneous or multiple measurements of plasma-free or urinary CA and MNs levels in the basal state and during the onset of hypertension, the diagnostic coincidence rate of PPGL can be further impr oved.[293,294,299,300]

In clinical practice, it is necessary to interpret the test results in combination with MN detection methods, patient status (diet, stress, activity, etc.), and other factors.

Clinical Question 35: How to Conduct a Tumor Localization Diagnosis for PPGL Patients?

Recommendations

We recommend computed tomography (CT) as the first choice of imaging modality to locate PPGL (1B).

We recommend magnetic resonance imaging (MRI) to detect skull base and neck paragangliomas (1C) in patients with metastatic PPGL.

We suggest the use of metaiodobenzylguanidine (MIBG) scintigraphy (1C), ^{68}Ga-Dotatate PET/CT scanning (2B), and somatostatin receptor imaging (2C) as functional imaging modalities in patients with metastatic PPGL.

Evidence and rationale

CT has been widely used in clinical practice. It is a non-invasive imaging examination with contrast that provides an excellent initial method for the localization of PPGLs in the thorax, abdomen, and pelvis, and the detection of pulmonary metastatic lesions.[6,30,46,47,293–295] In a systematic review providing information on adrenal washout CT on diagnostic performance, the pooled sensitivity and specificity for differentiating adenoma from pheochromocytoma was 0.97 (95% CI: 0.93–0.99) and 0.67 (95% CI: 0.44–0.84), respectively.[302] MRI is recommended for patients with metastatic PPGLs, for the detection of skull base and neck paragangliomas; patients with metal

artifacts when using CT; patients with an allergy to CT contrast; and for patients in whom radiation exposure should be limited (children, pregnant women, patients with known germline mutations, and those with recent excessive radiation exposure).[6,30,46,47,293–295]

MIBG is an adrenergic nerve blocker, similar to norepinephrine in structure, absorbed and stored by vesicles of tumors. ^{131}I- or ^{123}I-labeled MIBG scintigraphy is recommended as a functional and positional imaging modality for the detection of PPGLs. The sensitivity and specificity of ^{131}I-MIBG scintigraphy range from 78% to 83% and 100% for PPGLs, respectively. The sensitivity of ^{123}I-MIBG ranges between 85% and 88% for pheochromocytomas, and between 56% and 75% for paragangliomas, whereas the specificity ranges from 70% to 100% and 84% to 100%, respectively. In patients with metastatic PPGLs, or those for whom surgery is not an option, ^{131}I-MIBG scintigraphy is useful, if positive, and treatment with ^{131}I-MIBG may be considered in accordance with the functional and anatomical localization of the tumor.[46,47,293,294]

A portion of PPGLs have high expression of somatostatin receptors; therefore, radioisotope-labeled somatostatin analogs are used for molecular imaging of PPGLs with high sensitivity. ^{68}Ga-Dotatate is a radionuclide ^{68}Ga-labeled somatostatin analog that specifically binds to the somatostatin receptor on the PPGL tumor cell membrane. The sensitivity of ^{68}Ga-Dotatate PET/CT scanning for pheochromocytomas and paragangliomas is 97.4% and 95.8%, respectively.[293] An initial systematic review showed a superiority of ^{68}Ga-labeled somatostatin analog imaging compared with that via CT/MRI, ^{18}F-FDOPA PET, ^{18}F-FDG PET, and MIBG scintigraphy for the detection of PPGLs and metastatic PPGLs.[303,304] Compared with ^{131}I-MIBG scintigraphy, ^{68}Ga-Dotatate PET/CT shows a higher accuracy for populations with a high risk of metastasis and family syndromic features in PPGLs.[305] In clinical practice, owing to higher feasibility, MIBG scintigraphy is preferred.

Clinical Question 36: Which PPGL Patients should be Recommended for Genetic Testing?

Recommendations

We recommend that all patients with PPGLs should be engaged in shared decision-making for genetic testing, especially those with multifocal, metastatic, bilateral disease, a positive family history, or family syndromic features (2C).

Evidence and rationale

PPGLs are correlated with disease-causing gene mutations. More than 20 different PPGL susceptibility genes have been reported, but new ones are still being studied. Approximately 50% of PPGL patients are associated with genetic mutations.[293,294] The highest frequencies of gene mutations are *VHL*, *RET*, *NF1*, *TMEM127*, and *MAX* in patients with pheochromocytoma, most of which are bilateral adrenal tumors. The *RET* gene mutation is observed in patients with multiple endocrine neoplasia type 2. *SDHB* and *FH* mutations often indicate metastatic paraganglioma.[293]

Germline mutations in the subtypes of succinate dehydrogenase *SDHx* genes are associated with familial paraganglioma hereditary syndrome and other solid tumors such as gastrointestinal stromal tumors, renal carcinoma, and pituitary adenoma. These mutations are transmitted in an autosomal dominant manner for *SDHA*, *SDHB*, and *SDHC* genes, and with paternal transmission for *SDHD* and *SDHAF2* genes.[293,294,306] A systematic review showed that an *SDHB* mutation was correlated with PPGL metastasis (OR = 5.68 [95% CI: 1.79–18.06]), but not with PPGL location.[307] The incidence of metastatic PPGL was high in SDHB carriers (36.8%), and almost a quarter of patients with apparently sporadic PPGL harbored germline variants of the targeted genes.[308]

Clinical Question 37: What Type of Hypertensive Patients should be Screened for Renal Artery Stenosis (RAS)?

Recommendations

RAS screening should be considered if hypertensive patients meet one of the following conditions: (1) a history of atherosclerotic CVD (2C); (2) early onset hypertension (<40 years old) (2D); (3) continuous BP ≥160/100 mmHg, or a negative change from good previous BP control, independent of any changes to antihypertensive drugs or any other causes (GPS); (4) normal LVEF in conjunction with transient pulmonary edema (2D); (5) refractory hypertension (2C); (6) periumbilical vascular murmur (GPS) detected on physical examination; (7) significant increase of serum creatinine or significant decrease of BP after the use of antihypertensive drugs (especially ACEI/ARB) (2D); (8) unilateral renal atrophy (GPS); (9) hypokalemia (GPS).

Evidence and rationale

It is suggested that RAS is one of the important causes of hypertension. It is caused mostly by atherosclerosis and is more common in older patients. In young patients, it is mainly caused by diseases such as renal artery fibromuscular dysplasia, Takayasu arteritis, etc.[309] The detection rate of RAS in hypertensive populations is approximately 1.6–8.0%.[310] The clinical manifestations of RAS are not highly specific, presenting mostly as resistant hypertension and the progressive deterioration of renal function. A 2009 Dutch systematic review showed that the detection rate of RAS was 25.3% (95% CI: 23.6–27.0%) in patients with aortic or peripheral vascular disease and 17.8% (95% CI: 15.4–20.6%) in patients with hypertension and coronary atherosclerosis.[311] The detection rate of RAS is particularly high in adolescent hypertensive patients. A cross-sectional study in China in 2019 showed that RAS was the second most common secondary cause of hypertension in adolescents, accounting for 17.9% of secondary hypertension and 5.1% of all adolescent hypertension.

Hence, the proportion of RAS is high in relation to the overall hypertensive population.[312] Previous prospective cohort studies have shown that the detection rate of RAS in patients with resistant hypertension is up to 20%.[313] A 2014 RCT showed that RAS patients treated with ACEI/ARB had lower SBP ([148 ± 23] mmHg *vs.* [152 ± 23] mmHg, P <0.01) and were more likely to achieve BP targets (30% *vs.* 22%, P = 0.01) than patients treated with other medications.[314] According to a cross-sectional study in 2009,[315] pulmonary edema was detected in 6.9% of patients with RAS ≥50% and in 1.4% of patients with RAS <50% or with normal RAS values (P <0.01). Among other recommendations, no consistent systematic reviews/meta-analyses or original studies were retrieved. The recommendations are based on existing guidelines[29,30,196,316] and expert opinions.

Clinical Question 38: Which Tests are Recommended for the Diagnosis of RAS?

Recommendations

For patients with eGFR ≥30 mL·min^{-1}·1.73 m^{-2}, renal artery computed tomography angiography (CTA) is recommended as the first choice. Gadolinium-enhanced magnetic resonance angiography (MRA) and ultrasonography are alternative modalities (1B).

For patients with eGFR <30 mL·min^{-1}·1.73 m^{-2}, ultrasonography is recommended as the first choice, and non-enhanced magnetic resonance angiography (MRA) is recommended as an alternative. CTA or contrast-enhanced MRA should be avoided (GPS).

Digital subtraction angiography (DSA) remains the gold standard for the diagnosis of RAS. DSA may be considered when RAS is highly suspected and the results of non-invasive examinations are inconclusive, or when a revascularization is planned.

Captopril renal scintigraphy may be considered in those without obvious renal dysfunction (eGFR ≥60 mL·min^{-1}·1.73 m^{-2}) (2C).

Evidence and rationale

Renal artery CTA, ultrasonography, and MRA are all effective modalities for the anatomical diagnosis of RAS. A systematic review showed that in patients with suspected RAS, the area under the ROC curve was 0.99 for CTA, 0.99 for gadolinium-enhanced MRA, 0.97 for non-gadolinium-enhanced MRA, 0.93 for ultrasonography, 0.92 for captopril renal scintigraphy, and 0.72 for the captopril test[317] (measured by renin activity after administrating captopril), indicating that the diagnostic performances of CTA and contrast-enhanced MRA were closely matched and significantly better than other modalities. Another systematic review also suggested that both the contrast-enhanced MRA and CTA provided satisfactory accuracy in diagnosing RAS.[318] As for the comparison between MRA with and without gadolinium enhancement, a systematic review showed that the sensitivity and specificity for diagnosing RAS were 94% and 85% with non-enhanced MRA, and 97% and 93%[319] with gadolinium-enhanced MRA, respectively, suggesting the better specificity and positive predictive value of the latter. A systematic review evaluated the diagnostic performance of duplex ultrasonography for RAS by four parameters: peak systolic velocity, acceleration time, acceleration index in renal artery systolic period, and renal–aortic ratio. This study revealed that ultrasonography is a moderately accurate screening test for RAS, and that the peak systolic velocity had the highest performance.[320]

In patients with severe renal dysfunction (eGFR <30 mL·min^{-1}·1.73 m^{-2}), consensus panels have recommended caution against CTA or contrast-enhanced MRA, since they may increase the risks of contrast-induced nephropathy and nephrogenic systemic fibrosis. Ultrasonography and non-enhanced MRA are recommended for such patients, and the former is of priority because of its high accuracy, convenience, and low cost.

DSA is a feasible modality with which to detect the small branch stenosis of the renal artery, which tends to be undetectable via routine imaging examinations. A single-center study compared the efficacy of CTA, MRA, and DSA for detecting RAS among 402 suspected patients. The κ values were 0.59–0.64 for CTA and 0.40–0.51 for MRA. The combined sensitivity and specificity were 64% (95% CI: 55–73%) and 92% (95% CI: 90–95%) for CTA, and 62% (95% CI: 54–71%) and 84% (95% CI: 81–87%) for MRA, respectively.[321] These results indicate the insufficient repeatability and sensitivity of CTA and MRA to rule out RAS, with DSA remaining the gold standard diagnostic method for RAS diagnosis. Of note, DSA is not routinely recommended for diagnosing RAS owing to its invasiveness and high cost but should be considered when RAS cannot be confirmed via non-invasive examinations, or when a renovascular intervention is planned.

Captopril renal scintigraphy can indicate whether RAS is hemodynamically significant – providing additional information aside from CTA or MRA – and can help confirm the RAS from different aspects, especially in patients with questionable results from routine imaging examinations. This method is highly accurate in patients without obvious renal dysfunction (eGFR ≥60 mL·min^{-1}·1.73 m^{-2}), but is less effective in those with impaired renal function. A systematic review containing 12 studies and 2291 subjects found that the sensitivity and specificity of captopril renal scintigraphy for diagnosing RAS were 92.5% and 92.2%, respectively.[322] It should be noted that this method may increase the incidence of acute renal injury in patients with bilateral RAS, and the merits and demerits should be weighed before clinical decisions are made.

Clinical Question 39: Is RASI Recommended for BP Control in Hypertensive Patients with RAS?

Recommendations

RASI is recommended for the treatment of hypertension associated with unilateral RAS, under close monitoring

of urine output, serum electrolytes, and serum creatinine (1C).

RASI should be considered in RAS patients after successful revascularization (2C).

RASI may be cautiously initiated at a low dose under close monitoring of renal function in patients with bilateral RAS, solitary kidney, or single functioning kidney when other indications for RASI are present (2D).

Dosage reduction or discontinuation is recommended if oliguria occurs, or serum creatinine rises >0.5 mg/dL (44 μmol/L) or >30% from the baseline during RASI therapy (GPS).

Evidence and rationale

RASI (including ACEI and ARB) is the first-line drug for hypertension management. Compared to patients not receiving RASI, it is more effective in reducing BP, improving cardiovascular and renal prognosis (10.0 events/100 patient-years *vs*. 13.0 events/100 patient-years, HR = 0.70, 95% CI: 0.59–0.82),[323] and prolonging overall life expectancy in RAS patients.[324] Conversely, there is a potential risk of increased acute renal failure (1.2 events/100 patient-years *vs*. 0.6 events/100 patient-years, HR = 1.87, 95% CI: 1.05–3.33).[323] A previous study showed that RASI was effective and safe for hypertension control in patients with RAS.[325] Another study documented that most RASI-induced acute kidney injuries occur at the early stage of treatment, and that renal function recovered in most cases after the termination of the drug.[326]

Currently, international guidelines generally recommend RASI to control hypertension associated with unilateral RAS.[46,47,327] However, their referred clinical studies vary in the degree of stenosis of enrolled RAS patients; hence, consensus on which degree of unilateral RAS should be treated with RASI has not been established. A clinical decision of RASI therapy warrants a comprehensive consideration of patients' compliance and the feasibility of regular tests of renal function and serum electrolytes. Informing patients about the potential risk of renal function deterioration and obtaining their consent are also warranted before RASI initiation.

Whether RASI can be used in hypertensive patients with bilateral RAS, a solitary kidney, or a single-functioning kidney remains controversial in current guidelines.[327–329] An individualized evaluation of the patient's condition is necessary. In the baseline analysis of the CORAL (The Cardiovascular Outcomes in Renal Atherosclerotic Lesions) study, the administration of RASI was comparable between patients with bilateral and unilateral RAS (P = 0.38).[314] In a prospective cohort study, 78.3% of 69 patients with bilateral RAS >60% could tolerate ARBs without difficulty.[330] RASI is not absolutely contraindicated in patients with bilateral RAS. Therapy may be initiated at a low dosage, under regular monitoring of renal function, serum electrolytes, and urine output, especially during the initial stage of treatment. In patients with bilateral asymmetric RAS following RASI treatment, the decrease in the eGFR of the kidney with severe stenosis may be compensated for by the contralateral side. Thus, the overall eGFR and/or serum creatinine may not reflect changes in bilateral renal function timely and accurately. Therefore, isotope nephrography is recommended to monitor changes in split renal function before and throughout RASI treatment, if available.[331]

Percutaneous balloon angioplasty and stents contribute to the safety of RASI treatment in certain RAS patients.[332] A retrospective study found that in bilateral RAS patients following successful renal artery stent revascularization, 72% of patients were safely maintained on a target dose of ACEIs, while the remaining switched to ARB or other antihypertensives because of cough or baseline renal insufficiency. Importantly, no patient discontinued RASI owing to renal function deterioration. This study also showed that bilateral RAS patients combined with left ventricular failure or diabetes can safely tolerate long-term RASI therapy after successful renal artery stent revascularization.[333]

This guideline recommends the use of RASI in certain hypertension patients with RAS who meet specific indications, which should not be interpreted as encouraging RASI treatment in all RAS patients. It is necessary to take RAS severity, baseline renal function, comorbidities, economic status, and the feasibility of regular examination into comprehensive consideration before an individualized treatment plan is formulated.

Clinical Question 40: Is Medical or Interventional Therapy Recommended for Patients with Atherosclerotic Renal Artery Stenosis (ARAS)?

Recommendations

Medical therapy is primarily recommended in patients with ARAS (1B).

In ARAS patients with resistant hypertension, renal dysfunction, flash pulmonary edema, or refractory HF, interventional therapy may be considered (2D).

In patients with ARAS ≥70% and stenosis-related hypertension or renal function deterioration, interventional therapy should be considered (GPS).

Evidence and rationale

RAS is one of the most common causes of secondary hypertension[334]; and the prevalence of ARAS was 5–10% among the general population.[335] In ARAS patients, the combination use of antihypertensives, statins, and antiplatelet drugs did not increase the risks of refractory hypertension, renal function deterioration, or cardiovascular events compared with that via interventional therapy. Effective medical therapy can reduce invasive operations and complications in such populations. However, some ARAS patients who would benefit more from interventional therapy may miss their best opportunities owing to invalid recognition.

The 2017 ACC/AHA Hypertension Guidelines stated that medical therapy is the first choice for adults with ARAS.

Revascularization may be considered for those for whom medical therapy has failed (i.e., refractory hypertension, worsening renal function, and/or intractable HF).[6] The 2017 ESC and the European Society of Vascular Surgery (ESVS) guidelines decreased the recommendation class of revascularization in ARAS patients to III (IIb in 2011 guideline), recommending balloon angioplasty in selected patients with unexplained recurrent congestive HF or sudden pulmonary edema.[327]

The results of Cochrane's systematic review published in 2014 showed that compared with medical therapy, interventional therapy was associated with a greater reduction in DBP (MD = –2.00 mmHg, 95% CI: –3.72 mmHg to –0.27 mmHg), as well as in the amounts of antihypertensive drugs (MD = –0.18, 95% CI: –0.34 to –0.03). However, improvements in SBP (MD = –1.07 mmHg, 95% CI: –3.45 mmHg to 1.30 mmHg) and serum creatinine levels (MD = –7.99 μmol/L, 95% CI: –22.6 μmol/L to 6.62 μmol/L) were not significantly reduced between the two groups, and no differences were observed in cardiovascular events (OR = 0.91, 95% CI: 0.75–1.11) and renal events (OR = 1.02, 95% CI: 0.7–1.38).[332] Another systematic review published in 2021 showed that the addition of percutaneous transluminal renal angioplasty significantly reduced the incidence of resistant hypertension in comparison to that via the best medical therapy alone (OR = 0.09, 95% CI: 0.01–0.70). However, there was no significant reduction in the rates of stroke (OR = 0.87, 95% CI: 0.57–1.34) and all-cause mortality (OR = 0.93, 95% CI: 0.74–1.16).[336] Of note, the 2022 AHA scientific statement pointed out important limitations of current RCTs that compared the efficacy of renal revascularization with medical therapy. Collectively, these trials had loose criteria for revascularization eligibility and high rates of post-procedure complications, which may have resulted in an underestimation of the benefits of interventional therapy.[337] Studies show that revascularization, compared to medical therapy, tends to reduce the risk of death in RAS patients with HF (HR = 0.76, 95% CI: 0.58–0.99),[338] and in those with acute pulmonary edema (HR = 0.43, 95% CI: 0.20–0.91). Approximately 76% of patients have no recurrence of pulmonary edema following successful revascularization.[339,340] For RAS patients with renal function deterioration and resistant hypertension, interventional therapy (*vs.* medical therapy) is associated with a reduced risk of death (HR = 0.15, 95% CI: 0.02–0.94) and cardiovascular events (HR = 0.28, 95% CI: 0.10–0.79).[339] Little relevant evidence has been retrieved regarding whether interventional therapy should be recommended for patients with RAS ≥70% and for whom hypertension or renal dysfunction are proven to be stenosis-related. Current guidelines and expert consensus recommend aggressive intervention in patients with RAS ≥70% and stenosis-related hypertension or/and renal function deterioration, especially when more than one of the following indications are met: (1) The eGFR or blood flow on the diseased side decreases by >25% compared to that on the contralateral side; (2) The renal vein renin level on the diseased side is more than two times higher than that on the contralateral side; (3) A positive result of captopril stimulated radioisotope renal dynamic imaging is obtained; (4) The volume of the diseased kidney is smaller than that on the contralateral side.

Clinical Question 41: Is Continuous Positive Airway Pressure (CPAP) and MRA Therapy Recommended for Hypertensive Patients with Obstructive Sleep Apnea (OSA)?

Recommendations

CPAP during sleep is suggested for hypertensive patients with moderate to severe OSA (2C).

Mineral corticoid receptor antagonists are suggested for patients with moderate to severe OSA complicated with resistant hypertension (2C).

Evidence and rationale

Currently, non-invasive positive airway pressure therapy is the most effective method for treating OSA in adults, as well as the preferred treatment for patients with moderate to severe OSA (apnea–hypopnea index ≥15 times/h during sleep)[341] or symptomatic OSA, with CPAP being the most commonly used. Several international guidelines since 2019 have recommended that patients with hypertension complicated by OSA should consider CPAP therapy.[46,342,343] A systematic review in 2022 showed that after three months of treatment with CPAP, the 24-h mean BP (SBP: WMD = –5.01, 95% CI: –6.94 to –3.08; DBP: WMD = –3.30, 95% CI: –4.32 to –2.28), daytime mean BP (SBP: WMD = –4.34, 95% CI: –6.27 to –2.40; DBP: WMD = –2.97, 95% CI: –3.99 to –1.95), nighttime mean BP (SBP: WMD = –3.55, 95% CI: –5.08 to –2.03; DBP: WMD = –2.33, 95% CI: –3.27 to –1.40), and OBPM (SBP: WMD = –3.67, 95% CI: –5.76 to –1.58; DBP: WMD = –2.61, 95% CI: –4.88 to –0.71)[344] of patients with OSA and hypertension were all significantly reduced. A meta-analysis in 2020 showed that CPAP treatment did not improve cardiovascular prognosis including MACE (RR = 0.87, 95% CI: 0.70–1.10), cardiovascular-related death (RR = 0.94, 95% CI: 0.62–1.43), and myocardial infarction (RR = 1.04, 95% CI: 0.79–1.37).[345] Another meta-analysis in 2023 found that improving adherence to CPAP therapy could reduce the risk of recurrent major adverse cardiac and cerebrovascular events in adults with CVD and OSA, highlighting its importance in secondary cardiovascular prevention in patients with OSA.[346]

Clinically, before beginning CPAP therapy, patients must undergo a thorough assessment of their nasal and lung conditions to investigate any possible underlying illness that may be contributing to, or exacerbating OSA, and have the treatment fully explained. During treatment, the proper nasal or oronasal mask should be chosen, and the appropriate titration pressures should be maintained. The result of long-term follow-up necessitates periodic adjustments to the CPAP titration pressures.

The incidence of both OSA and hyperaldosteronism is very high in patients with resistant hypertension.[347] A significant positive correlation between plasma aldosterone level and OSA severity is observed in patients with resistant hypertension[348,349] but not in non-resistant hypertensive subjects.[348] MRA (including spironolactone and eplerenone) may reduce the severity of OSA by reducing water and sodium retention, which is appropriate for

OSA patients with resistant hypertension who do not receive or are unable to tolerate CPAP treatment. A rapid systematic review including two RCTs demonstrated that MRA significantly decreased the apnea–hypopnea index (MD = −16.12, 95% CI: −23.05 to −9.19), ABPM mean BP (24-h mean SBP: MD = −7.60, 95% CI: −12.71 to −2.49; 24-h mean DBP: MD = −8.79, 95% CI: −13.98 to −3.59; daytime mean SBP: MD = −8.12, 95% CI: −15.34 to −0.91; daytime mean DBP: MD = −6.99, 95% CI: −12.14 to −1.83; nighttime mean SBP: MD = −14.59, 95% CI: −17.57 to −11.60; nighttime mean DBP: MD = −11.33, 95% CI: −20.49 to −2.16), and OBPM levels (office SBP: MD = −9.79, 95% CI: −16.49 to −3.09; office DBP: MD = −3.67, 95% CI: −6.33 to −1.02).[350,351]

There are currently no RCTs comparing MRA with other diuretics, and the efficacy of MRA in patients with mild OSA and non-resistant hypertension is unclear. In the future, larger studies on the use of MRA in OSA patients with hypertension should be conducted to further demonstrate its efficacy.

Clinical Question 42: Which Hypertensive Patients are Recommended for Genetic Testing to Exclude Monogenic Hypertension?

Recommendations

Hypertensive patients with onset age ≤35 years, abnormal blood potassium, a low plasma renin level, and common secondary hypertension excluded are recommended for genetic testing to screen for monogenic hypertension (2D).

Evidence and rationale

Monogenic hypertension is defined as the Mendelian inherited forms of hypertension, and the main clinical characteristics are early onset, abnormal blood potassium level, and low plasma renin level.[352,353] Liddle syndrome is the most common type of monogenic hypertension,[354] while other types are rare. Genetic testing is the gold standard for diagnosing monogenic hypertension. Some types of monogenic hypertension may be addressed with effective targeted treatment after diagnosis. Conversely, if the diagnosis is missed or delayed, it may cause serious target organ damage and a poor prognosis. So far, a high-quality study of gene diagnosis of monogenic hypertension is lacking, and there are only cross-sectional studies and case series studies. A Chinese single-center cross-sectional study (n = 766) in 2019 conducted gene testing on hypertensive patients with onset age ≤40 years, with common secondary hypertension excluded. This study reported a Liddle syndrome prevalence of 0.91% in the cohort.[354] A Chinese multicenter cross-sectional study (n = 1179) in 2020 examined the variants in hypertensive patients ≤35 years of age or with abnormal blood potassium, hormone levels, and imaging features. The results showed that 33 patients (2.8%) carried 21 different pathogenic or possible pathogenic variants.[355] Additionally, there are some case series studies and case reports published in recent years that confirm early age of onset, abnormal blood potassium levels, and low plasma renin levels as the main features of monogenic hypertension.[355,356] As the overall prevalence of monogenic hypertension is low, and the current cost of gene testing is not cheap and not covered by national medical insurance, we recommend genetic testing for hypertensive patients with age of onset ≤35 years of age, abnormal blood potassium, low plasma renin level, and common secondary hypertension excluded. Since the technical threshold still remains in genetic detection and interpretation, we recommend that gene testing be performed in experienced centers.

Clinical Question 43: Which Assessment Tools are Recommended for the Screening of Depression and Anxiety in Patients with Hypertension?

Recommendations

The patient health questionnaire-9 (PHQ-9) is recommended for the screening of depressive symptoms in patients with hypertension (2B).

The generalized anxiety disorder-7 (GAD-7) is recommended for the screening of anxiety symptoms in patients with hypertension (2B).

Evidence and rationale

Depression and anxiety are associated with levels of BP and medication compliance in patients with hypertension and are also highly prevalent risk factors for CVDs.[357,358] The systematic reviews published in JAMA (2023) on depression and anxiety screening in primary care settings for asymptomatic adults aged 19–64 years found that using the PHQ-9 for depression screening with a cutoff score of ≥10 resulted in a sensitivity of 0.85 (95% CI: 0.79–0.89) and a specificity of 0.85 (95% CI: 0.82–0.88).[359] For anxiety screening, the use of the GAD-7 with a cutoff score of ≥10, resulted in a pooled sensitivity of 0.79 (95% CI: 0.65–0.94), a heterogeneity of I^2 = 77.3%, and a pooled specificity of 0.89 (95% CI: 0.83–0.94) with a heterogeneity of I^2 = 94.8%.[360] PHQ-9 and GAD-7 are self-reported measures of symptoms of depression and anxiety, respectively. Symptoms with scores of 10 or greater in the past two weeks are considered clinically significant. We recommend joint screening of depression and anxiety. Timely psychological interventions are needed for patients with these symptoms. Exercise, music, and mindfulness are recommended in everyday life to maintain mental health. If necessary, patients should be advised to visit a psychologist or a psychiatrist.

Clinical Question 44: For Hypertensive Patients with Comorbid Depression or Anxiety, is a Combination of Antihypertensive Medications and Antidepressants/Anxiolytics Recommended?

Recommendations

For hypertensive patients with comorbid depression or anxiety, a combination of antihypertensive medication and antidepressants/anxiolytics is recommended (2C).

Evidence and rationale

Depression is independently related to stroke and cardiovascular events.[361] Depression and anxiety may activate the autonomic nervous system and lead to an increase in heart rate and BP.[362] The recommendation for combining antidepressants/anxiolytics with antihypertensive medication is inconsistent across different guidelines. Our group conducted a meta-analysis and a total of six RCTs (n = 729)[363–368] were included. The results suggested that a combination treatment with antihypertensive medication and antidepressants/anxiolytics significantly reduced SBP (MD = 11.42 mmHg, 95% CI: 6.53–16.31 mmHg) and DBP (MD = 6.23 mmHg, 95% CI: 2.91–9.55 mmHg) compared to treatment with antihypertensive medication alone. Another RCT[368,369] that included older patients with hypertension, but not included in the meta-analysis, also revealed significant reductions in BP in the combination treatment group in comparison to the group on antihypertensive medication alone. However, the number of relevant studies is small, and the heterogeneity is high; therefore, the interpretation of the results requires caution. Additionally, the drug–drug interactions need to be fully considered before combining antihypertensive medications and antidepressants/anxiolytics.[370] Selective serotonin reuptake inhibitors (SSRIs, i.e., escitalopram) have a small impact on BP and should be used under the guidance of a psychiatrist. Excessive antihypertensive therapy needs to be avoided in patients with white-coat hypertension. Patients with severe depressive or anxiety symptoms or those who have a history of psychiatric disorders should be advised to visit a psychiatric clinic.

Gaps in the Evidence and the Need for Further Studies

This guideline currently lacks robust evidence-based medical support for certain clinical issues, and several questions in clinical practice remain to be addressed. The questions are summarized as follows, providing direction for future research on hypertension.

1) BP measurement and risk evaluation:

• The optimal SBP and DBP levels at different time points in life.

• Incremental accuracy of risk estimation in terms of short- and long-term BP variability.

• Optimal interval for the reassessment of BP in non-hypertensive patients.

• What are the optimal BP treatment targets according to HBPM and ABPM?

• Validity and the application of cuffless BP measurement devices.

• Optimal BP measurement methods and interpretation of BP values in AF.

2) For patients with SBP 130–139 mmHg and/or DBP 80–89 mmHg:

• Do they need antihypertensive drug treatment?

• When to start antihypertensive drug treatment?

• Are they likely to comply with lifestyle interventions, and how effective are these interventions?

3) Treatment strategies:

• Optimal time-point and BP level to initiate treatment in young patients.

• Optimal and safe BP thresholds and targets in very old (≥80 years) and frail hypertensive patients.

• Office *vs.* out-of-office guided treatment on clinical outcomes.

• BP thresholds and targets in low-to-moderate-risk individuals.

• BP thresholds and targets in specific patient groups (left ventricular hypertrophy, diabetes mellitus, CKD, isolated systolic hypertension, HF including HFrEF and HFpEF) and stroke patients.

• Treatment effect on clinical outcomes in mask hypertension and white-coat hypertension.

• Effect of lifestyle interventions on CV outcomes.

• Strategies to implement lifestyle recommendations effectively.

• Choice of first-line antihypertensive agent and sequence of titration from a population and individual level perspective.

• Effectiveness and implementation strategies for individualized antihypertensive treatment.

• Effect of device-based therapy (RDN) on CV and kidney outcomes.

• Effects of down-titration and treatment withdrawal in different clinical settings.

• Feasibility, resources, and cost–benefit evaluations of intensive BP lowering treatment in clinical practice.

• Optimal antihypertensive agents for hypertensive patients with a history of stroke or TIA.

• Outcome-based comparisons of BP treatment with classical *vs.* vasodilator beta-blockers.

• Impact of single-pill *vs.* multidrug treatment strategies on adherence to treatment, BP control, and clinical outcomes.

• Effect of antihypertensive therapy on cognitive function in older patients.

4) Follow-up

• Optimal timing and frequency of follow-up.

• Effect of distance monitoring and digital alert systems on clinical outcomes for hypertensive patients.

• Evaluation of and interventions to improve adherence.

The key recommendations from this guideline are synthesized to establish a clinical pathway for hypertension management [Figure 1].

Guideline Drafting Institutions and Members

Clinical chairman

Jun Cai, Beijing Anzhen Hospital, Capital Medical University

Methodology chairman

Yaolong Chen, Research Unit of Evidence-Based Evaluation and Guidelines, Chinese Academy of Medical Sciences, School of Basic Medical Sciences, Lanzhou University

Guideline Advisory Committee

Runlin Gao, Department of cardiology, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences; Dayi Hu, Institute of Cardiovascular Disease, People's Hospital of Peking University; Yaling Han, Department of Cardiology, General Hospital of Northern Theater Command; Junbo Ge, Department of Cardiology, Zhongshan Hospital, Fudan University; Yun Zhang, Department of Cardiology, Qilu Hospital, Shandong University; Changsheng Ma, Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University; Rutai Hui, Hypertension Center, Fuwai Hospital, Chinese Academy of Medical Sciences; Lianyou Zhao, Department of Cardiology, Tangdu Hospital, Air Force Military Medical University.

Guideline Development Group (listed in order of the strokes of the last name)

Peili Bu, Department of Cardiovascular Medicine, Qilu Hospital, Shandong University; Wenjun Ma, Hypertension Center, Fuwai Hospital, Chinese Academy of Medical Sciences; Mei Wang, Department of National Fitness and Scientific Exercise Research Center, China Institute of Sport Science; Jin Bian, Hypertension Center, Fuwai Hospital, Chinese Academy of Medical Sciences; Xinhua Yin, Department of Cardiovascular Medicine, General Hospital, Shenzhen University; Xinzheng Lu, Department of Cardiovascular Medicine, the First Affiliated Hospital of Nanjing Medical University; Gang Tian, Department of Cardiovascular Medicine, the First Affiliated Hospital of Xi'an Jiaotong University; Yingqing Feng, Cardiovascular Disease Center, Guangdong Provincial People's Hospital; Ming Ren, Department of Cardiovascular Medicine, Affiliated Hospital of Qinghai University; Qi Hua,

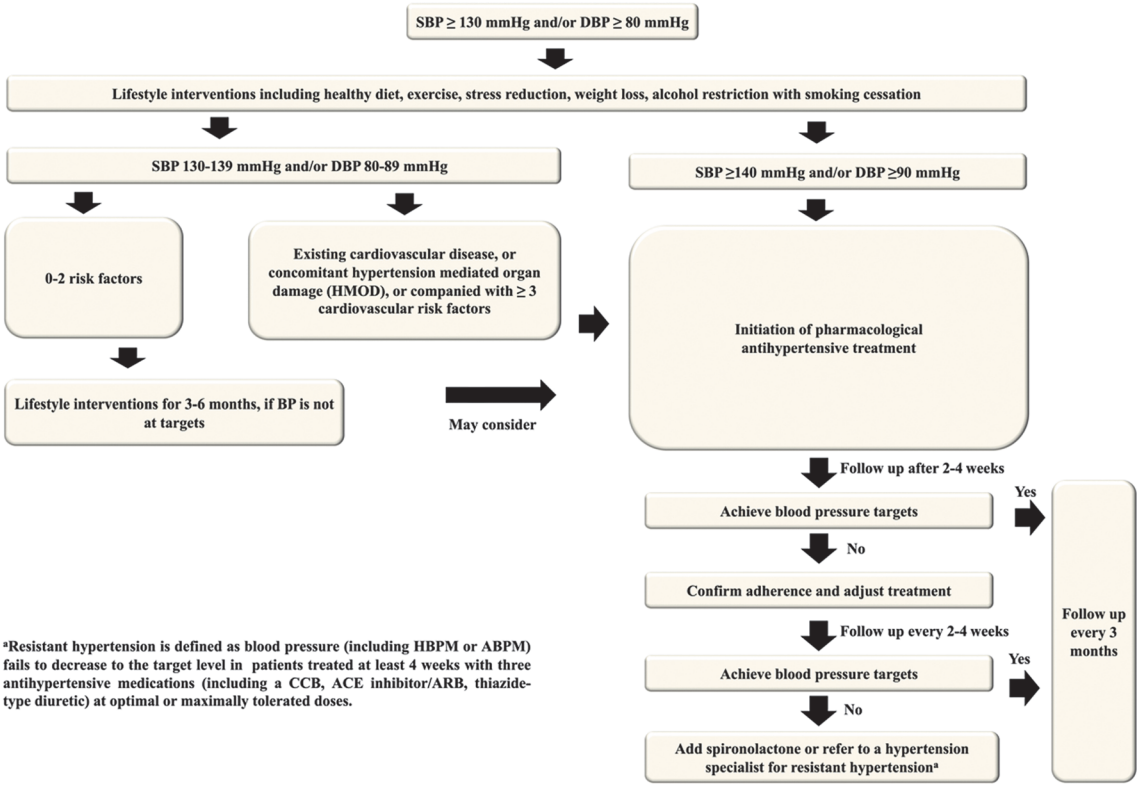

Figure 1: Diagnosis and treatment path diagram of hypertension. ABPM: Ambulatory BP monitoring; ACE: Angiotensin-converting enzyme; ARB: Angiotensin-receptor blocker; BP: Blood pressure; CCB: Calcium-channel blocker; DBP: Diastolic blood pressure; HBPM: Home BP monitoring; SBP: Systolic blood pressure.

Department of Cardiology, Xuanwu Hospital, Capital Medical University; Quan Liu, Department of Cardiology, the First Hospital of Jilin University; Kejun Liu, China National Health Development Research Center; Lihong Liu, Department of Pharmacy, China-Japan Friendship Hospital; Min Liu, Department of Hypertension, Henan Provincial People's Hospital; Wei Liu, Department of Cardiovascular Medicine, Beijing Hospital; Gang Sun, Department of Hypertension, the Second Affiliated Hospital of Baotou Medical College; Yingxian Sun, Department of Cardiology, the First Hospital of China Medical University; Jianjun Mou, Department of Cardiovascular Medicine, the First Affiliated Hospital of Xi'an Jiaotong University; Xiaowei Yan, Department of Cardiovascular Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences; Yuming Li, Department of Hypertension, Tianjin Kanghui Hospital; Qifu Li, Department of Endocrinology, the First Affiliated Hospital of Chongqing Medical University; Yongjun Li, Department of Vascular Surgery, Beijing Hospital; Nanfang Li, Department of Hypertension, People's Hospital of Xinjiang Uygur Autonomous Region; Yong Li, Department of Cardiology, Huashan Hospital Fudan University; Ping Li, Department of Cardiovascular Medicine, the Second Affiliated Hospital of Nanchang University; Jinfeng Yang, Department of Cardiology, Jizhou District People's Hospital, Tianjin; Yanmin Yang, Emergency Center of Fuwai Hospital, Chinese Academy of Medical Sciences; Shouling Wu, Department of Cardiology, Kailuan General Hospital; Zhong Wu, Department of Cardiovascular Medicine, Hainan Provincial People's Hospital; Hao Wu, School of General Medicine and Continuing Education, Capital Medical University; Haiying Wu, Hypertension Center, Fuwai Hospital, Chinese Academy of Medical Sciences; Jing Yu, Hypertension Center, Lanzhou University Second Hospital; Daowen Wang, Department of Cardiovascular Medicine, Tongji Hospital, Huazhong University of Science and Technology; Lei Song, Cardiomyopathy Ward, Fuwai Hospital, Chinese Academy of Medical Sciences; Hongwei Zhang, Department of Cardiology, Shunyi District Hospital, Beijing; Huimin Zhang, Hypertension Center, Fuwai Hospital, Chinese Academy of Medical Sciences; Youren Chen, Department of Cardiology, the Second Affiliated Hospital of Shantou University Medical College; Fang Chen, Heart Diagnosis and Treatment Center of Yinchuan First People's Hospital; Xiaoping Chen, Department of Cardiology, West China Hospital, Sichuan University; Weihua Yue, Peking University Sixth Hospital, Peking University Institute of Mental Health; Birong Zhou, Department of Cardiovascular Medicine, First Affiliated Hospital of Anhui Medical University; Dong Zhao, Clinical and Epidemiologic Research Center, Beijing Anzhen Hospital, Capital Medical University; Qiuping Zhao, Department of Hypertension, Central Cardiovascular Hospital, Fuwai Hospital; Xiaolong Zhao, Department of Endocrinology and Metabolism, Shanghai Public Health Clinical Center; Wei Yu, Hypertension Center of Zhejiang Hospital; Yinong Jiang, Department of Cardiology, the First Affiliated Hospital of Dalian Medical University; Zhiming Zhu, Department of Hypertension and Endocrinology, Daping Hospital, Army Military Medical University; Lan Yao, School of Medicine and Health Management, Tongji Medical College, Huazhong University of Science and Technology; Hong Yuan, Clinical Trial Research Center of the Third Xiangya Hospital of Central South University; Xinjuan Xu, Department of Hypertension, Heart Center, the First Affiliated Hospital of Xinjiang Medical University; Zihong Guo, Hypertension Center, Fuwai Cardiovascular Hospital, Yunnan Province; Yifang Guo, Department of Geriatric Cardiology, Hebei Gereral Hospital; Jun Tao, Department of Cardiology, the First Affiliated Hospital of Sun Yat-sen University; Jing Huang, Department of Cardiovascular Medicine, the Second Affiliated Hospital of Chongqing Medical University; Zhaoqiang Cui, Department of Cardiology, the Affiliated Zhongshan Hospital; Shaobo Jiang, Department of Urology, Shandong Provincial Hospital Affiliated to Shandong First Medical University; Xiongjing Jiang, Vascular Surgery Center, Fuwai Hospital, Chinese Academy of Medical Sciences; Qinghua Han, Department of Cardiology, First Hospital of Shanxi Medical University; Chunyu Zeng, Department of Cardiovascular Medicine, Army Characteristic Medical Center; Liangdi Xie, Department of Cardiology, the First Affiliated Hospital of Fujian Medical University; Guangyan Cai, Department of Nephrology, the First Medical Center of PLA General Hospital.

Evidence Review Group (listed in order of the strokes of the last name)

Ying Shan, Department of Cardiology, Huashan Hospital Fudan University; Qingfeng Ma, Department of Neurology, Xuanwu Hospital, Capital Medical University; Zijun Wang, Institute of Health Data Science, Lanzhou University; Lu Wang, Beijing Anzhen Hospital, Capital Medical University; Quan Shen, Affiliated Children's Hospital of Chongqing Medical University; Qianling Shi, Institute of Health Data Science, Lanzhou University; Bo Bian, Department of General Medicine, Tianjin Medical University General Hospital; Aijun Xing, Department of Cardiology, Kailuan General Hospital; Jie Ren, Department of Cardiology, Shanxi Bethune Hospital; Mengjuan Ren, School of Public Health, Lanzhou University; Yunlan Liu, School of Public Health, Lanzhou University; Kai Liu, Department of Cardiology, Fuwai Hospital, Chinese Academy of Medical Sciences; Xiao Liu, School of Public Health, Lanzhou University; Hui Liu, Evidence-based Medicine Center, School of Basic Medical Sciences, Lanzhou University; Yue Qi, Clinical and Epidemiologic Research Center, Beijing Anzhen Hospital, Capital Medical University; Runmin Sun, Hypertension Center, Lanzhou University Second Hospital; Yajia Sun, School of Public Health, Lanzhou University; Yaoyao Sun, Peking University Sixth Hospital, Peking University Institute of Mental Health; Renfeng Su, School of Public Health, Lanzhou University; Jinzi Su, Department of Cardiology, the First Affiliated Hospital of Fujian Medical University; Xin Du, Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University; Shicheng Li, Department of Cardiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences; Zhao Li, Department of Cardiology, the First Hospital of China Medical University; Ning Yang, Department of Hypertension, Tianjin Kanghui Hospital; Yaling Yang, Department of

Endocrinology and Metabolism, Shanghai Public Health Clinical Center; Lirui Yang, Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University; Xiaomin Yang, Department of General Practice, Sir Run Run Shaw Hospital affiliated to Zhejiang University; Nan Yang, Institute of Health Data Science, Lanzhou University; Shouyuan Wu, School of Public Health, Lanzhou University; Yubao Zou, Department of Cardiology, Fuwai Hospital, Chinese Academy of Medical Sciences; Wei Song, Department of Cardiology, the First Affiliated Hospital of Dalian Medical University; Tao Zhang, Emergency Center of Fuwai Hospital, Chinese Academy of Medical Sciences; Yao Lu, Clinical Trial Research Center of the Third Xiangya Hospital, Central South University; Zuoquan Chen, Department of Vascular Surgery, Beijing Hospital; Gailing Chen, Department of Cardiology, China-Japan Friendship Hospital; Chaoqun Fan, Department of National Fitness and Scientific Exercise Research Center, China Institute of Sport Science; Xiaoyang Zhou, Department of Cardiology, Renmin Hospital of Wuhan University; Ying Zheng, Department of Nephrology, the First Medical Center of PLA General Hospital; Junxian Zhao, School of Public Health, Lanzhou University; Jinbo Hu, Department of Endocrinology, the First Affiliated Hospital of Chongqing Medical University; Tianchun Hou, Laboratory of Children's Excellence Evidence in Children's Hospital of Chongqing Medical University, Coordinating with the Guidelines; Ying Lou, Department of Cardiology, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Science; Lixia Yao, Department of Geriatric Cardiology, Hebei Gereral Hospital; Ning Suo, Department of Urology, Shandong Provincial Hospital Affiliated to Shandong First Medical University; Ainan Jia, National Center for Chronic and Non-Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention; Wenhao Xia, Department of Hypertension and Vascular Diseases, the First Affiliated Hospital of Sun Yat-sen University; Qiangqiang Guo, School of Public Health, Lanzhou University; Zhengrong Huang, Department of Cardiology, the First Affiliated Hospital of Xiamen University; Qiang Peng, Department of Cardiology, the Second Affiliated Hospital of Nanchang University; Ruobing Lei, National Clinical Research Center for Children's Health and Disease; Lianman He, Department of Hypertension, Henan Provincial People's Hospital.

External Review Group

Tzung-Dau Wang, Department of Cardiology, Hospital affiliated to the Medical College of Taiwan University, China; Xinchun Yang, Heart Center of Beijing Chaoyang Hospital Affiliated to Capital Medical University; Hong Chen, Department of Cardiology, Peking University People's Hospital.

References

1. Wang Z, Chen Z, Zhang L, Wang X, Hao G, Zhang Z, *et al*. Status of hypertension in China: Results from the China hypertension survey, 2012-2015. Circulation 2018;137:2344–2356. doi: 10.1161/CIRCULATIONAHA.117.032380.
2. The Writing Committee of the Annual Report on Cardiovascular Health and Diseases in China. Interpretation of the annual report on cardiovascular health and diseases in China 2022. Cardiol Discovery 2024;4:58–80. doi: 10.1097/cd9.0000000000000119.
3. McEvoy JW, McCarthy CP, Bruno RM, Brouwers S, Canavan MD, Ceconi C, *et al*. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. Eur Heart J 2024;45:3912–4018. doi: 10.1093/eurheartj/ehae178.
4. Guideline for the pharmacological treatment of hypertension in adults. Geneva: World Health Organization, 2021. Available from: https://www.who.int/publications/i/item/9789240033986. [Last accessed on 2024].
5. Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, *et al*. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension. J Hypertens 2023;41:1874–2071. doi: 10.1097/hjh.0000000000003480.
6. Whelton PK, Carey RM, Aronow WS, Casey DE Jr., Collins KJ, Dennison Himmelfarb C, *et al*. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2018;138:e426–e483. doi: 10.1161/CIR.0000000000000597.
7. Lou Y, Ma WJ, Wang ZJ, Cai J, Sun YX, Li YM, *et al*. China hypertension clinical practice guidelines proposal (in Chinese). Chin J Cardiol 2022;50:671–675.
8. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, *et al*. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011;64:401–406. doi: 10.1016/j.jclinepi.2010.07.015.
9. Guyatt GH, Alonso-Coello P, Schünemann HJ, Djulbegovic B, Nothacker M, Lange S, *et al*. Guideline panels should seldom make good practice statements: Guidance from the GRADE Working Group. J Clin Epidemiol 2016;80:3–7. doi: 10.1016/j.jclinepi.2016.07.006.
10. Qi Y, Han X, Zhao D, Wang W, Wang M, Sun J, *et al*. Long-term cardiovascular risk associated with stage 1 hypertension defined by the 2017 ACC/AHA hypertension guideline. J Am Coll Cardiol 2018;72:1201–1210. doi: 10.1016/j.jacc.2018.06.056.
11. Wu S, Xu Y, Zheng R, Lu J, Li M, Chen L, *et al*. Hypertension defined by 2017 ACC/AHA guideline, ideal cardiovascular health metrics, and risk of cardiovascular disease: A nationwide prospective cohort study. Lancet Reg Health West Pac 2022;20:100350. doi: 10.1016/j.lanwpc.2021.100350.
12. Li LX, Zhu CR, Lin LM, Li HY, Wei YM, Du X, *et al*. The effect of different blood pressure levels on the risk of early-onset stroke in a young population (in Chinese). Chin J Hypertens 2022;30:1061–1068.
13. Peng X, Jin C, Song Q, Wu S, Cai J. Stage 1 hypertension and the 10-year and lifetime risk of cardiovascular disease: A prospective real-world study. J Am Heart Assoc 2023;12:e028762. doi: 10.1161/JAHA.122.028762.
14. Gu D, Chen J, Wu X, Duan X, Jones DW, Huang JF, *et al*. Prehypertension and risk of cardiovascular disease in Chinese adults. J Hypertens 2009;27:721–729. doi: 10.1097/HJH.0b013e328323ad89.
15. Han M, Chen Q, Liu L, Li Q, Ren Y, Zhao Y, *et al*. Stage 1 hypertension by the 2017 American College of Cardiology/American Heart Association hypertension guidelines and risk of cardiovascular disease events: Systematic review, meta-analysis, and estimation of population etiologic fraction of prospective cohort studies. J Hypertens 2020;38:573–578. doi: 10.1097/hjh.0000000000002321.
16. Luo D, Cheng Y, Zhang H, Ba M, Chen P, Li H, *et al*. Association between high blood pressure and long term cardiovascular events in young adults: Systematic review and meta-analysis. BMJ 2020;370:m3222. doi: 10.1136/bmj.m3222.
17. Sergi G, Dianin M, Bertocco A, Zanforlini BM, Curreri C, Mazzochin M, *et al*. Gender differences in the impact of metabolic syndrome components on mortality in older people: A systematic review and meta-analysis. Nutr Metab Cardiovasc Dis 2020;30:1452–1464. doi: 10.1016/j.numecd.2020.04.034.
18. Zheng Y, Xie Z, Li J, Chen C, Cai W, Dong Y, *et al*. Meta-analysis of metabolic syndrome and its individual components with risk of atrial fibrillation in different populations. BMC Cardiovasc Disord 2021;21:90. doi: 10.1186/s12872-021-01858-1.

19. Global report on hypertension: The race against a silent killer. Geneva: World Health Organization, 2023. Available from: https://www.who.int/publications/i/item/9789240081062. [Last accessed on 2024].
20. Cao X, Zhao Z, Kang Y, Tian Y, Song Y, Wang L, *et al*. The burden of cardiovascular disease attributable to high systolic blood pressure across China, 2005-18: A population-based study. Lancet Public Health 2022;7:e1027–e1040. doi: 10.1016/S2468-2667(22)00232-8.
21. Blood Pressure Lowering Treatment Trialists' Collaboration. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: An individual participant-level data meta-analysis. Lancet 2021;397:1625–1636. doi: 10.1016/S0140-6736(21)00590-0.
22. Blood Pressure Lowering Treatment Trialists' Collaboration. Age-stratified and blood-pressure-stratified effects of blood-pressure-lowering pharmacotherapy for the prevention of cardiovascular disease and death: An individual participant-level data meta-analysis. Lancet 2021;398:1053–1064. doi: 10.1016/S0140-6736(21)01921-8.
23. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: Meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ 2009;338:b1665. doi: 10.1136/bmj.b1665.
24. Law MR, Wald NJ, Morris JK, Jordan RE. Value of low dose combination treatment with blood pressure lowering drugs: Analysis of 354 randomised trials. BMJ 2003;326:1427. doi: 10.1136/bmj.326.7404.1427.
25. Suchard MA, Schuemie MJ, Krumholz HM, You SC, Chen R, Pratt N, *et al*. Comprehensive comparative effectiveness and safety of first-line antihypertensive drug classes: A systematic, multinational, large-scale analysis. Lancet 2019;394:1816–1826. doi: 10.1016/S0140-6736(19)32317-7.
26. Wiysonge CS, Bradley H, Mayosi BM, Maroney R, Mbewu A, Opie LH, *et al*. Beta-blockers for hypertension. Cochrane Database Syst Rev 2007:CD002003. doi: 10.1002/14651858.CD002003.pub2.
27. Zhong XL, Dong Y, Xu W, Huang YY, Wang HF, Zhang TS, *et al*. Role of blood pressure management in stroke prevention: A systematic review and network meta-analysis of 93 randomized controlled trials. J Stroke 2021;23:1–11. doi: 10.5853/jos.2020.02698.
28. Gu D, He J, Coxson PG, Rasmussen PW, Huang C, Thanataveerat A, *et al*. The cost-effectiveness of low-cost essential antihypertensive medicines for hypertension control in China: A modelling study. PLoS Med 2015;12:e1001860. doi: 10.1371/journal.pmed.1001860.
29. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, *et al*. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021–3104. doi: 10.1093/eurheartj/ehy339.
30. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, *et al*. 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension 2020;75:1334–1357. doi: 10.1161/HYPERTENSIONAHA.120.15026.
31. State council measures to enhance people's fitness, health. The State Council, 2019. Available from: http://english.www.gov.cn/policies/latestreleases/201907/15/content_WS5d2c6f8fc6d05cbd94d67a02.html. [Last accessed on 2024].
32. Chinese Society of Cardiology of Chinese Medical Association, Cardiovascular Disease Prevention and Rehabilitation Committee of Chinese Association of Rehabilitation Medicine, Cardiovascular Disease Committee of Chinese Association of Gerontology and Geriatrics, Thrombosis Prevention and Treatment Committee of Chinese Medical Doctor Association. Guidelines for primary prevention of cardiovascular disease in China (in Chinese). Chin J Cardiol 2020;48:1000–1038. doi: 10.3760/cma.j.cn112148-20201009-00796.
33. Brunström M, Carlberg B. Benefits and harms of lower blood pressure treatment targets: Systematic review and meta-analysis of randomised placebo-controlled trials. BMJ Open 2019;9:e026686. doi: 10.1136/bmjopen-2018-026686.
34. Li J, Zhao D, Cai J, Chen S, Wu S, Qi Y. Cost-effectiveness of treatment in adults with blood pressure of 130–139/80–89 mmHg and high cardiovascular risk in China: A modelling study. Lancet Reg Health West Pac 2023;42:100962. doi: 10.1016/j.lanwpc.2023.100962.
35. Liu J, Wang W, Liu J, Qi Y, Sun JY, Zhao D. Comorbid cardiovascular disease risk factors and blood pressure control in outpatients with hypertensive disease (in Chinese). Chin J Cardiol 2013;41:1050–1054. doi: 10.3760/cma.j.issn.0253-3758.2013.12.014.
36. Ohta Y, Tsuchihashi T, Onaka U, Hasegawa E. Clustering of cardiovascular risk factors and blood pressure control status in hypertensive patients. Intern Med 2010;49:1483–1487. doi: 10.2169/internalmedicine.49.3406.
37. Cuspidi C, Rescaldani M, Sala C. Prevalence of echocardiographic left-atrial enlargement in hypertension: A systematic review of recent clinical studies. Am J Hypertens 2013;26:456–464. doi: 10.1093/ajh/hpt001.
38. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, *et al*. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599–3726. doi: 10.1093/eurheartj/ehab368.
39. Overvad TF, Nielsen PB, Larsen TB, Søgaard P. Left atrial size and risk of stroke in patients in sinus rhythm. A systematic review. Thromb Haemost 2016;116:206–219. doi: 10.1160/TH15-12-0923.
40. Rossi A, Temporelli PL, Quintana M, Dini FL, Ghio S, Hillis GS, *et al*. Independent relationship of left atrial size and mortality in patients with heart failure: An individual patient meta-analysis of longitudinal data (MeRGE Heart Failure). Eur J Heart Fail 2009;11:929–936. doi: 10.1093/eurjhf/hfp112.
41. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. Am J Cardiol 2002;90:1284–1289. doi: 10.1016/s0002-9149(02)02864-3.
42. Ohkuma T, Tomiyama H, Ninomiya T, Kario K, Hoshide S, Kita Y, *et al*. Proposed cutoff value of brachial-ankle pulse wave velocity for the management of hypertension. Circ J 2017;81:1540–1542. doi: 10.1253/circj.CJ-17-0636.
43. Asayama K, Ohkubo T, Hoshide S, Kario K, Ohya Y, Rakugi H, *et al*. From mercury sphygmomanometer to electric device on blood pressure measurement: Correspondence of Minamata Convention on Mercury. Hypertens Res 2016;39:179–182. doi: 10.1038/hr.2015.158.
44. Park SH, Park YS. Can an automatic oscillometric device replace a mercury sphygmomanometer on blood pressure measurement? A systematic review and meta-analysis. Blood Press Monit 2019;24:265–276. doi: 10.1097/MBP.0000000000000412.
45. Stergiou GS, Alpert B, Mieke S, Asmar R, Atkins N, Eckert S, *et al*. A universal standard for the validation of blood pressure measuring devices: Association for the Advancement of Medical Instrumentation/European Society of Hypertension/International Organization for Standardization (AAMI/ESH/ISO) Collaboration Statement. J Hypertens 2018;36:472–478. doi: 10.1097/HJH.0000000000001634.
46. Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, *et al*. The Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2019). Hypertens Res 2019;42:1235–1481. doi: 10.1038/s41440-019-0284-9.
47. Rabi DM, McBrien KA, Sapir-Pichhadze R, Nakhla M, Ahmed SB, Dumanski SM, *et al*. Hypertension Canada's 2020 comprehensive guidelines for the prevention, diagnosis, risk assessment, and treatment of hypertension in adults and children. Can J Cardiol 2020;36:596–624. doi: 10.1016/j.cjca.2020.02.086.
48. Kallioinen N, Hill A, Horswill MS, Ward HE, Watson MO. Sources of inaccuracy in the measurement of adult patients' resting blood pressure in clinical settings. J Hypertens 2017;35:421–441. doi: 10.1097/HJH.0000000000001197.
49. Brady TM, Charleston J, Ishigami J, Miller ER, Matsushita K, Appel LJ. Effects of different rest period durations prior to blood pressure measurement: The best rest trial. Hypertension 2021;78:1511–1519. doi: 10.1161/hypertensionaha.121.17496.
50. Stergiou GS, Palatini P, Parati G, O'Brien E, Januszewicz A, Lurbe E, *et al*. 2021 European Society of Hypertension practice guidelines for office and out-of-office blood pressure measurement. J Hypertens 2021;39:1293–1302. doi: 10.1097/HJH.0000000000002843.
51. Irving G, Holden J, Stevens R, McManus RJ. Which cuff should I use? Indirect blood pressure measurement for the diagnosis of hypertension in patients with obesity: A diagnostic accuracy review. BMJ Open 2016;6:e012429. doi: 10.1136/bmjopen-2016-012429.
52. Seguret D, Gamelon D, Dourmap C, Steichen O. Blood pressure measurements on a bare arm, over a sleeve or below a rolled-up

sleeve: A systematic review and meta-analysis. J Hypertens 2020;38:1650–1658. doi: 10.1097/HJH.0000000000002460.
53. Beaney T, Burrell LM, Castillo RR, Charchar FJ, Cro S, Damasceno A, *et al*. May Measurement Month 2018: A pragmatic global screening campaign to raise awareness of blood pressure by the International Society of Hypertension. Eur Heart J 2019;40:2006–2017. doi: 10.1093/eurheartj/ehz300.
54. Kakkar AK, Mueller I, Bassand JP, Fitzmaurice DA, Goldhaber SZ, Goto S, *et al*. Risk profiles and antithrombotic treatment of patients newly diagnosed with atrial fibrillation at risk of stroke: Perspectives from the international, observational, prospective GARFIELD registry. PLoS One 2013;8:e63479. doi: 10.1371/journal.pone.0063479.
55. Pagonas N, Schmidt S, Eysel J, Compton F, Hoffmann C, Seibert F, *et al*. Impact of atrial fibrillation on the accuracy of oscillometric blood pressure monitoring. Hypertension 2013;62:579–584. doi: 10.1161/hypertensionaha.113.01426.
56. Viera AJ, Yano Y, Lin FC, Simel DL, Yun J, Dave G, *et al*. Does this adult patient have hypertension?: The rational clinical examination systematic review. JAMA 2021;326:339–347. doi: 10.1001/jama.2021.4533.
57. Bo Y, Kwok KO, Chung VC, Yu CP, Tsoi KK, Wong SY, *et al*. Short-term reproducibility of ambulatory blood pressure measurements: A systematic review and meta-analysis of 35 observational studies. J Hypertens 2020;38:2095–2109. doi: 10.1097/HJH.0000000000002522.
58. Kang YY, Li Y, Huang QF, Song J, Shan XL, Dou Y, *et al*. Accuracy of home versus ambulatory blood pressure monitoring in the diagnosis of white-coat and masked hypertension. J Hypertens 2015;33:1580–1587. doi: 10.1097/HJH.0000000000000596.
59. Cheng YB, Thijs L, Zhang ZY, Kikuya M, Yang WY, Melgarejo JD, *et al*. Outcome-driven thresholds for ambulatory blood pressure based on the new American College of Cardiology/American Heart Association classification of hypertension. Hypertension 2019;74:776–783. doi: 10.1161/HYPERTENSIONAHA.119.13512.
60. Vongpatanasin W, Ayers C, Lodhi H, Das SR, Berry JD, Khera A, *et al*. Diagnostic thresholds for blood pressure measured at home in the context of the 2017 hypertension guideline. Hypertension 2018;72:1312–1319. doi: 10.1161/HYPERTENSIONAHA.118.11657.
61. Yang WY, Melgarejo JD, Thijs L, Zhang ZY, Boggia J, Wei FF, *et al*. Association of office and ambulatory blood pressure with mortality and cardiovascular outcomes. JAMA 2019;322:409–420. doi: 10.1001/jama.2019.9811.
62. Stergiou GS, Siontis KC, Ioannidis JP. Home blood pressure as a cardiovascular outcome predictor: It's time to take this method seriously. Hypertension 2010;55:1301–1303. doi: 10.1161/HYPERTENSIONAHA.110.150771.
63. Parati G, Stergiou G, O'Brien E, Asmar R, Beilin L, Bilo G, *et al*. European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. J Hypertens 2014;32:1359–1366. doi: 10.1097/HJH.0000000000000221.
64. Sheppard JP, Tucker KL, Davison WJ, Stevens R, Aekplakorn W, Bosworth HB, *et al*. Self-monitoring of blood pressure in patients with hypertension-related multi-morbidity: Systematic review and individual patient data meta-analysis. Am J Hypertens 2020;33:243–251. doi: 10.1093/ajh/hpz182.
65. van Onzenoort HA, Verberk WJ, Kroon AA, Kessels AG, Nelemans PJ, van der Kuy PH, *et al*. Effect of self-measurement of blood pressure on adherence to treatment in patients with mild-to-moderate hypertension. J Hypertens 2010;28:622–627. doi: 10.1097/HJH.0b013e328334f36b.
66. Shimbo D, Artinian NT, Basile JN, Krakoff LR, Margolis KL, Rakotz MK, *et al*. Self-measured blood pressure monitoring at home: A joint policy statement from the American Heart Association and American Medical Association. Circulation 2020;142:e42–e63. doi: 10.1161/CIR.0000000000000803.
67. Juhanoja EP, Johansson JK, Puukka PJ, Jula AM, Niiranen TJ. Optimal schedule for assessing home BP variability: The Finn-Home Study. Am J Hypertens 2018;31:715–725. doi: 10.1093/ajh/hpy030.
68. Hodgkinson JA, Stevens R, Grant S, Mant J, Bray EP, Hobbs FDR, *et al*. Schedules for self-monitoring blood pressure: A systematic review. Am J Hypertens 2019;32:350–364. doi: 10.1093/ajh/hpy185.
69. Fujiwara T, Hoshide S, Nishizawa M, Matsuo T, Kario K. Difference in evening home blood pressure between before dinner and at bedtime in Japanese elderly hypertensive patients. J Clin Hypertens (Greenwich) 2017;19:731–739. doi: 10.1111/jch.12985.
70. Bayó J, Dalfo A, Barceló MA, Saez M, Roca C, Pallozzi J, *et al*. The role first-day readings play in a 3-day schedule of self-monitoring home blood pressure based on prognostic data. VAMPAHICA study. Am J Hypertens 2020;33:154–160. doi: 10.1093/ajh/hpz178.
71. Chin BH, Beh HC, Ching SM, Devaraj NK, Chia YC. A13859 Discarding the first day's home blood pressure measurements. J Hypertens 2018;36:e219–e220. doi: 10.1097/01.hjh.0000548897.09322.90.
72. Juhanoja EP, Puukka PJ, Johansson JK, Niiranen TJ, Jula AM. The impact of the day of the week on home blood pressure: The Finn-Home Study. Blood Press Monit 2016;21:63–68. doi: 10.1097/MBP.0000000000000156.
73. Fu J, Liu Y, Zhang L, Zhou L, Li D, Quan H, *et al*. Nonpharmacologic interventions for reducing blood pressure in adults with prehypertension to established hypertension. J Am Heart Assoc 2020;9:e016804. doi: 10.1161/jaha.120.016804.
74. Krishnamoorthy Y, Nagarajan R, Murali S. Effectiveness of multiple combined lifestyle interventions in reducing blood pressure among patients with prehypertension and hypertension: A network meta-analysis. J Public Health (Oxf) 2023;45:e319–e331. doi: 10.1093/pubmed/fdac027.
75. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, *et al*. 2019 ACC/AHA Guideline on the primary prevention of cardiovascular disease: A report of the American College of Cardiology/American Heart Association Task force on clinical practice guidelines. Circulation 2019;140:e596–e646. doi: 10.1161/CIR.0000000000000678.
76. Tay JC, Sule AA, Chew EK, Tey JS, Lau T, Lee S, *et al*. Ministry of Health clinical practice guidelines: Hypertension. Singapore Med J 2018;59:17–27. doi: 10.11622/smedj.2018007.
77. Diabetes and hypertension care for adults in primary care settings. Food and Health Bureau, 2022. Available from: https://www.fhb.gov.hk/pho/files/primary_care_settings_eng.pdf. [Last accessed on 2024].
78. Filippini T, Malavolti M, Whelton PK, Vinceti M. Sodium intake and risk of hypertension: A systematic review and dose-response meta-analysis of observational cohort studies. Curr Hypertens Rep 2022;24:133–144. doi: 10.1007/s11906-022-01182-9.
79. Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, *et al*. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med 2001;344:3–10. doi: 10.1056/NEJM200101043440101.
80. Geleijnse JM, Kok FJ, Grobbee DE. Blood pressure response to changes in sodium and potassium intake: A metaregression analysis of randomised trials. J Hum Hypertens 2003;17:471–480. doi: 10.1038/sj.jhh.1001575.
81. National Health Commission. Report on nutrition and chronic diseases in China (2020) (in Chinese). ACTA Nutrimenta SINICA 2020;42:521.
82. He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ 2013;346:f1325. doi: 10.1136/bmj.f1325.
83. Anderson CA, Appel LJ, Okuda N, Brown IJ, Chan Q, Zhao L, *et al*. Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: The INTERMAP study. J Am Diet Assoc 2010;110:736–745. doi: 10.1016/j.jada.2010.02.007.
84. Neal B, Wu Y, Feng X, Zhang R, Zhang Y, Shi J, *et al*. Effect of salt substitution on cardiovascular events and death. N Engl J Med 2021;385:1067–1077. doi: 10.1056/NEJMoa2105675.
85. Yuan Y, Jin A, Neal B, Feng X, Qiao Q, Wang H, *et al*. Salt substitution and salt-supply restriction for lowering blood pressure in elderly care facilities: A cluster-randomized trial. Nat Med 2023;29:973–981. doi: 10.1038/s41591-023-02286-8.
86. Aburto NJ, Hanson S, Gutierrez H, Hooper L, Elliott P, Cappuccio FP. Effect of increased potassium intake on cardiovascular risk factors and disease: Systematic review and meta-analyses. BMJ 2013;346:f1378. doi: 10.1136/bmj.f1378.
87. Vinceti M, Filippini T, Crippa A, de Sesmaisons A, Wise LA, Orsini N. Meta-analysis of potassium intake and the risk of stroke. J Am Heart Assoc 2016;5:e004210. doi: 10.1161/JAHA.116.004210.
88. Ndanuko RN, Ibrahim R, Hapsari RA, Neale EP, Raubenheimer D, Charlton KE. Association between the urinary sodium to

potassium ratio and blood pressure in adults: A systematic review and meta-analysis. Adv Nutr 2021;12:1751–1767. doi: 10.1093/advances/nmab036.
89. Gonçalves C, Abreu S. Sodium and potassium intake and cardiovascular disease in older people: A systematic review. Nutrients 2020;12:3447. doi: 10.3390/nu12113447.
90. Hanssen H, Boardman H, Deiseroth A, Moholdt T, Simonenko M, Kränkel N, *et al*. Personalized exercise prescription in the prevention and treatment of arterial hypertension: A Consensus Document from the European Association of Preventive Cardiology (EAPC) and the ESC Council on Hypertension. Eur J Prev Cardiol 2022;29:205–215. doi: 10.1093/eurjpc/zwaa141.
91. Barone Gibbs B, Hivert MF, Jerome GJ, Kraus WE, Rosenkranz SK, Schorr EN, *et al*. Physical activity as a critical component of first-line treatment for elevated blood pressure or cholesterol: Who, what, and how?: A scientific statement from the American Heart Association. Hypertension 2021;78:e26–e37. doi: 10.1161/HYP.0000000000000196.
92. Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, *et al*. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. Eur Heart J 2021;42:17–96. doi: 10.1093/eurheartj/ehaa605.
93. Naci H, Salcher-Konrad M, Dias S, Blum MR, Sahoo SA, Nunan D, *et al*. How does exercise treatment compare with antihypertensive medications? A network meta analysis of 391 randomised controlled trials assessing exercise and medication effects on, systolic blood pressure. Br J Sports Med 2019;53:859–869. doi: 10.1136/bjsports-2018-099921.
94. Leal JM, Galliano LM, Del Vecchio FB. Effectiveness of high-intensity interval training versus moderate-intensity continuous training in hypertensive patients: A systematic review and meta-analysis. Curr Hypertens Rep 2020;22:26. doi: 10.1007/s11906-020-1030-z.
95. Chekroud SR, Gueorguieva R, Zheutlin AB, Paulus M, Krumholz HM, Krystal JH, *et al*. Association between physical exercise and mental health in 1.2 million individuals in the USA between 2011 and 2015: A cross-sectional study. Lancet Psychiatry 2018;5:739–746. doi: 10.1016/S2215-0366(18)30227-X.
96. Oja P, Kelly P, Pedisic Z, Titze S, Bauman A, Foster C, *et al*. Associations of specific types of sports and exercise with all-cause and cardiovascular-disease mortality: A cohort study of 80 306 British adults. Br J Sports Med 2017;51:812–817. doi: 10.1136/bjsports-2016-096822.
97. Deborah RJK, Gary L. American College of Sports Medicine. ACSM's Guidelines for exercise testing and prescription. 10th ed. Baltimore (MD): Lippincott Williams & Wilkins; 2016: 143–144.
98. Global BMI Mortality Collaboration; Di Angelantonio E, Bhupathiraju ShN, Wormser D, Gao P, Kaptoge S, *et al*. Body-mass index and all-cause mortality: Individual-participant-data meta-analysis of 239 prospective studies in four continents. Lancet 2016;388:776–786. doi: 10.1016/S0140-6736(16)30175-1.
99. Obesity Group of the Endocrinology Branch of the Chinese Medical Association. Expert consensus on prevention and treatment of adult obesity in China (in Chinese). Chin J Endocrinol Metab 2011;27:711–717. doi: 10.3760/cma.j.issn.1000-6699.2011.09.003.
100. Siebenhofer A, Winterholer S, Jeitler K, Horvath K, Berghold A, Krenn C, *et al*. Long-term effects of weight-reducing drugs in people with hypertension. Cochrane Database Syst Rev 2021;1:CD007654. doi: 10.1002/14651858.CD007654.pub5.
101. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, *et al*. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 2021;384:989–1002. doi: 10.1056/NEJMoa2032183.
102. Wadden TA, Bailey TS, Billings LK, Davies M, Frias JP, Koroleva A, *et al*. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: The STEP 3 randomized clinical trial. JAMA 2021;325:1403–1413. doi: 10.1001/jama.2021.1831.
103. Rubino D, Abrahamsson N, Davies M, Hesse D, Greenway FL, Jensen C, *et al*. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: The STEP 4 randomized clinical trial. JAMA 2021;325:1414–1425. doi: 10.1001/jama.2021.3224.
104. Garvey WT, Frias JP, Jastreboff AM, le Roux CW, Sattar N, Aizenberg D, *et al*. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): A double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet 2023;402:613–626. doi: 10.1016/S0140-6736(23)01200-X.
105. Zhao L, Cheng Z, Lu Y, Liu M, Chen H, Zhang M, *et al*. Tirzepatide for weight reduction in Chinese adults with obesity: The SURMOUNT CN randomized clinical trial. JAMA 2024;332:551–560. doi: 10.1001/jama.2024.9217.
106. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, *et al*. Semaglutide and cardiovascular outcomes in obesity without diabetes. N Engl J Med 2023;389:2221–2232. doi: 10.1056/NEJMoa2307563.
107. Wang L, Lin M, Yu J, Fan Z, Zhang S, Lin Y, *et al*. The impact of bariatric surgery versus non surgical treatment on blood pressure: Systematic review and meta analysis. Obes Surg 2021;31:4970–4984. doi: 10.1007/s11695-021-05671-9.
108. Wilhelm SM, Young J, Kale-Pradhan PB. Effect of bariatric surgery on hypertension: A meta-analysis. Ann Pharmacother 2014;48:674–682. doi: 10.1177/1060028014529260.
109. Thyroid and Metabolic Surgery Group of the Surgical Branch of the Chinese Medical Association, Committee of Obesity and Diabetes Surgeons of the Surgical Physicians Branch of the Chinese Medical Association. Guidelines for the surgical management of obesity and type 2 diabetes in China (2019 edition) (in Chinese). Chin J Pract Surg 2019;39:301–306. doi: 10.19538/j.cjps.issn1005-2208.2019.04.01.
110. van Veldhuisen SL, Gorter TM, van Woerden G, de Boer RA, Rienstra M, Hazebroek EJ, *et al*. Bariatric surgery and cardiovascular disease: A systematic review and meta-analysis. Eur Heart J 2022;43:1955–1969. doi: 10.1093/eurheartj/ehac071.
111. Brunström M, Carlberg B. Association of blood pressure lowering with mortality and cardiovascular disease across blood pressure levels: A systematic review and meta-analysis. JAMA Intern Med 2018;178:28–36. doi: 10.1001/jamainternmed.2017.6015.
112. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, *et al*. Blood pressure lowering for prevention of cardiovascular disease and death: A systematic review and meta-analysis. Lancet 2016;387:957–967. doi: 10.1016/S0140-6736(15)01225-8.
113. ACCORD Study Group; Cushman WC, Evans GW, Byington RP, Goff DC Jr., Grimm RH Jr., *et al*. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med 2010;362:1575–1585. doi: 10.1056/NEJMoa1001286.
114. SPRINT Research Group; Wright JT Jr., Williamson JD, Whelton PK, Snyder JK, Sink KM, *et al*. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015;373:2103–2116. doi: 10.1056/NEJMoa1511939.
115. Zhang W, Zhang S, Deng Y, Wu S, Ren J, Sun G, *et al*. Trial of intensive blood-pressure control in older patients with hypertension. N Engl J Med 2021;385:1268–1279. doi: 10.1056/NEJMoa2111437.
116. Yano Y, Stamler J, Garside DB, Daviglus ML, Franklin SS, Carnethon MR, *et al*. Isolated systolic hypertension in young and middle-aged adults and 31-year risk for cardiovascular mortality: The Chicago Heart Association Detection Project in Industry study. J Am Coll Cardiol 2015;65:327–335. doi: 10.1016/j.jacc.2014.10.060.
117. Son JS, Choi S, Kim K, Kim SM, Choi D, Lee G, *et al*. Association of blood pressure classification in Korean young adults according to the 2017 American College of Cardiology/American Heart Association guidelines with subsequent cardiovascular disease events. JAMA 2018;320:1783–1792. doi: 10.1001/jama.2018.16501.
118. Wu S, Song Y, Chen S, Zheng M, Ma Y, Cui L, *et al*. Blood pressure classification of 2017 associated with cardiovascular disease and mortality in young Chinese adults. Hypertension 2020;76:251–258. doi: 10.1161/HYPERTENSIONAHA.119.14239.
119. Julius S, Nesbitt SD, Egan BM, Weber MA, Michelson EL, Kaciroti N, *et al*. Feasibility of treating prehypertension with an angiotensin-receptor blocker. N Engl J Med 2006;354:1685–1697. doi: 10.1056/NEJMoa060838.
120. Fuchs SC, Poli-de-Figueiredo CE, Figueiredo Neto JA, Scala LC, Whelton PK, Mosele F, *et al*. Effectiveness of chlorthalidone plus amiloride for the prevention of hypertension: The PREVER-prevention randomized clinical trial. J Am Heart Assoc 2016;5:e004248. doi: 10.1161/JAHA.116.004248.
121. Lüders S, Schrader J, Berger J, Unger T, Zidek W, Böhm M, *et al*. The PHARAO study: Prevention of hypertension with the angiotensin-converting enzyme inhibitor ramipril in patients with high-normal blood pressure: A prospective, randomized, controlled

prevention trial of the German Hypertension League. J Hypertens 2008;26:1487–1496. doi: 10.1097/HJH.0b013e3282ff8864.
122. Verdecchia P, Staessen JA, Angeli F, de Simone G, Achilli A, Ganau A, *et al*. Usual versus tight control of systolic blood pressure in non-diabetic patients with hypertension (Cardio-Sis): An open-label randomised trial. Lancet 2009;374:525–533. doi: 10.1016/S0140-6736(09)61340-4.
123. SPS3 Study Group; Benavente OR, Coffey CS, Conwit R, Hart RG, McClure LA, *et al*. Blood-pressure targets in patients with recent lacunar stroke: The SPS3 randomised trial. Lancet 2013;382:507–515. doi: 10.1016/S0140-6736(13)60852-1.
124. Vaduganathan M, Claggett BL, Juraschek SP, Solomon SD. Assessment of long-term benefit of intensive blood pressure control on residual life span: Secondary Analysis of the Systolic Blood Pressure Intervention Trial (SPRINT). JAMA Cardiol 2020;5:576–581. doi: 10.1001/jamacardio.2019.6192.
125. Sun Y, Mu J, Wang DW, Ouyang N, Xing L, Guo X, *et al*. A village doctor led multifaceted intervention for blood pressure control in rural China: An open, cluster randomised trial. Lancet 2022;399:1964–1975. doi: 10.1016/S0140-6736(22)00325-7.
126. He J, Ouyang N, Guo X, Sun G, Li Z, Mu J, *et al*. Effectiveness of a non-physician community health-care provider led intensive blood pressure intervention versus usual care on cardiovascular disease (CRHCP): An open label, blinded endpoint, cluster randomised trial. Lancet 2023;401:928–938. doi: 10.1016/S0140-6736(22)02603-4.
127. Bangalore S, Toklu B, Gianos E, Schwartzbard A, Weintraub H, Ogedegbe G, *et al*. Optimal systolic blood pressure target after SPRINT: Insights from a network meta-analysis of randomized trials. Am J Med 2017;130:707–719.e8. doi: 10.1016/j.amjmed.2017.01.004.
128. Gorenek B, Pelliccia A, Benjamin EJ, Boriani G, Crijns HJ, Fogel RI, *et al*. European Heart Rhythm Association (EHRA)/European Association of Cardiovascular Prevention and Rehabilitation (EACPR) position paper on how to prevent atrial fibrillation endorsed by the Heart Rhythm Society (HRS) and Asia Pacific Heart Rhythm Society (APHRS). Europace 2017;19:190–225. doi: 10.1093/europace/euw242.
129. Du X, Ninomiya T, de Galan B, Abadir E, Chalmers J, Pillai A, *et al*. Risks of cardiovascular events and effects of routine blood pressure lowering among patients with type 2 diabetes and atrial fibrillation: Results of the ADVANCE study. Eur Heart J 2009;30:1128–1135. doi: 10.1093/eurheartj/ehp055.
130. Pinho-Gomes AC, Azevedo L, Copland E, Canoy D, Nazarzadeh M, Ramakrishnan R, *et al*. Blood pressure-lowering treatment for the prevention of cardiovascular events in patients with atrial fibrillation: An individual participant data meta-analysis. PLoS Med 2021;18:e1003599. doi: 10.1371/journal.pmed.1003599.
131. Kim D, Yang PS, Kim TH, Jang E, Shin H, Kim HY, *et al*. Ideal blood pressure in patients with atrial fibrillation. J Am Coll Cardiol 2018;72:1233–1245. doi: 10.1016/j.jacc.2018.05.076.
132. Kim D, Yang P-S, Jang E, Tae Yu H, Kim T-H, Uhm J-S, *et al*. Blood pressure control and dementia risk in midlife patients with atrial fibrillation. Hypertension 2020;75:1296–1304. doi: 10.1161/hypertensionaha.119.14388.
133. Kodani E, Atarashi H, Inoue H, Okumura K, Yamashita T, Otsuka T, *et al*. Impact of blood pressure control on thromboembolism and major hemorrhage in patients with nonvalvular atrial fibrillation: A subanalysis of the J-RHYTHM registry. J Am Heart Assoc 2016;5:e004075. doi: 10.1161/JAHA.116.004075.
134. National Center for Cardiovascular Disease, Office of Primary Hypertension Management of the National Basic Public Health Service Program, National Expert Committee on Primary Hypertension Management. National guidelines for primary hypertension prevention and management 2020 edition (in Chinese). Chin Circ J 2021;36:209–220.
135. Bundy JD, Li C, Stuchlik P, Bu X, Kelly TN, Mills KT, *et al*. Systolic blood pressure reduction and risk of cardiovascular disease and mortality: A systematic review and network meta-analysis. JAMA Cardiol 2017;2:775–781. doi: 10.1001/jamacardio.2017.1421.
136. Wokhlu A, Smith SM, Gong Y, Handberg EM, Elgendy IY, Bavry AA, *et al*. Mortality implications of lower DBP with lower achieved systolic pressures in coronary artery disease: Long-term mortality results from the INternational VErapamil-trandolapril STudy US cohort. J Hypertens 2018;36:419–427. doi: 10.1097/HJH.0000000000001559.
137. Bangalore S, Messerli FH, Wun CC, Zuckerman AL, DeMicco D, Kostis JB, *et al*. J-curve revisited: An analysis of blood pressure and cardiovascular events in the Treating to New Targets (TNT) Trial. Eur Heart J 2010;31:2897–2908. doi: 10.1093/eurheartj/ehq328.
138. Clinical practice guideline for adult hypertension-prevention, screening, counseling and management. 2024. Available from: https://www.managementmahealthcare.com/pdf/practice_guidelines/Hypertension.pdf. [Last accessed on 2024].
139. Sakima A, Satonaka H, Nishida N, Yatsu K, Arima H. Optimal blood pressure targets for patients with hypertension: A systematic review and meta-analysis. Hypertens Res 2019;42:483–495. doi: 10.1038/s41440-018-0123-4.
140. Kawano H, Fujiwara A, Kai H, Kumagai E, Okamoto R, Shibata R, *et al*. Effects of blood pressure lowering in patients with heart failure with preserved ejection fraction: A systematic review and meta-analysis. Hypertens Res 2019;42:504–513. doi: 10.1038/s41440-019-0216-8.
141. Fox CS, Golden SH, Anderson C, Bray GA, Burke LE, de Boer IH, *et al*. Update on prevention of cardiovascular disease in adults with type 2 diabetes mellitus in light of recent evidence: A scientific statement from the American Heart Association and the American Diabetes Association. Diabetes Care 2015;38:1777–1803. doi: 10.2337/dci15-0012.
142. American Diabetes Association Professional Practice Committee. 10. Cardiovascular disease and risk management: standards of care in diabetes-2024. Diabetes Care 2024;47(Suppl 1):S179–S218. doi: 10.2337/dc24-S010.
143. Joseph JJ, Deedwania P, Acharya T, Aguilar D, Bhatt DL, Chyun DA, *et al*. Comprehensive management of cardiovascular risk factors for adults with type 2 diabetes: A scientific statement from the American Heart Association. Circulation 2022;145:e722–e759. doi: 10.1161/cir.0000000000001040.
144. Aronow WS, Shamliyan TA. Blood pressure targets for hypertension in patients with type 2 diabetes. Ann Transl Med 2018;6:199. doi: 10.21037/atm.2018.04.36.
145. Brouwer TF, Vehmeijer JT, Kalkman DN, Berger WR, van den Born BH, Peters RJ, *et al*. Intensive blood pressure lowering in patients with and patients without type 2 diabetes: A pooled analysis from two randomized trials. Diabetes Care 2018;41:1142–1148. doi: 10.2337/dc17-1722.
146. White WB, Jalil F, Cushman WC, Bakris GL, Bergenstal R, Heller SR, *et al*. Average clinician' measured blood pressures and cardiovascular outcomes in patients with type 2 diabetes mellitus and ischemic heart disease in the EXAMINE trial. J Am Heart Assoc 2018;7:e009114. doi: 10.1161/JAHA.118.009114.
147. Li SN, Chen Z, Wang ZW. Analysis of the current situation of hypertension among the elderly in China (in Chinese). Chin J Hypertens 2019;27:140–148. doi: 10.16439/j.cnki.1673-7245.2019.02.002.
148. National institute for health and care excellence. 2023. Available from: https://www. nice. org.uk/guidance/NG136. [Last accessed on 2024].
149. Hua QFL, Li J, *et al*. Chinese guidelines for the management of hypertension in the elderly (in Chinese). Chin J Hypertens 2023;31:508–538. doi: 10.16439/j.issn.1673-7245.2023.06.003.
150. Chinese Society of Cardiovascular Disease Hypertension Group. Chinese expert recommendations for intensive blood pressure control (in Chinese). Chin J Hypertens 2022;30:113–117.
151. Stroke and transient ischaemic attack in over 16s: Diagnosis and initial management. National Institute for Health and Care Excellence (NICE); 2022. Available from: https://www.nice.org.uk/guidance/ng128. [Last accessed on 2024].
152. Li G, Lin Y, Yang J, Anderson CS, Chen C, Liu F, *et al*. Intensive ambulance-delivered blood-pressure reduction in hyperacute stroke. N Engl J of Med 2024;390:1862–1872. doi: 10.1056/NEJMoa2314741.
153. Qureshi AI, Palesch YY, Barsan WG, Hanley DF, Hsu CY, Martin RL, *et al*. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. N Engl J Med 2016;375:1033–1043. doi: 10.1056/NEJMoa1603460.
154. Leonardi-Bee J, Bath PM, Phillips SJ, Sandercock PA, IST Collaborative Group. Blood pressure and clinical outcomes in the International Stroke Trial. Stroke 2002;33:1315–1320. doi: 10.1161/01.str.0000014509.11540.66.
155. Bangalore S, Schwamm L, Smith EE, Hellkamp AS, Suter RE, Xian Y, *et al*. Blood pressure and in-hospital outcomes in patients presenting with ischaemic stroke. Eur Heart J 2017;38:2827–2835. doi: 10.1093/eurheartj/ehx330.

156. He WJ, Zhong C, Xu T, Wang D, Sun Y, Bu X, *et al*. Early antihypertensive treatment and clinical outcomes in acute ischemic stroke: Subgroup analysis by baseline blood pressure. J Hypertens 2018;36:1372–1381. doi: 10.1097/HJH.0000000000001690.
157. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, *et al*. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2019;50:e344–e418. doi: 10.1161/STR.0000000000000211.
158. Huang Q, Zhang JZ, Wu JA. Meta-analysis of blood pressure management in the acute phase of ischemic stroke (in Chinese). National Med J China 2018;98:1876–1881. doi: 10.3760/cma.j.issn.0376-2491.2018.23.015.
159. Ahmed N, Wahlgren N, Brainin M, Castillo J, Ford GA, Kaste M, *et al*. Relationship of blood pressure, antihypertensive therapy, and outcome in ischemic stroke treated with intravenous thrombolysis: Retrospective analysis from Safe Implementation of Thrombolysis in Stroke-International Stroke Thrombolysis Register (SITS-ISTR). Stroke 2009;40:2442–2449. doi: 10.1161/STROKEAHA.109.548602.
160. Lei Z, Li S, Hu S, Ren L. Effects of baseline systolic blood pressure on outcome in ischemic stroke patients with intravenous thrombolysis therapy: A systematic review and meta-analysis. Neurologist 2020;25:62–69. doi: 10.1097/NRL.0000000000000267.
161. Endo K, Kario K, Koga M, Nakagawara J, Shiokawa Y, Yamagami H, *et al*. Impact of early blood pressure variability on stroke outcomes after thrombolysis: The SAMURAI rt-PA Registry. Stroke 2013;44:816–818. doi: 10.1161/strokeaha.112.681007.
162. van den Berg SA, Uniken Venema SM, Mulder MJHL, Treurniet KM, Samuels N, Lingsma HF, *et al*. Admission blood pressure in relation to clinical outcomes and successful reperfusion after endovascular stroke treatment. Stroke 2020;51:3205–3214. doi: 10.1161/strokeaha.120.029907.
163. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, *et al*. Guidelines for adult stroke rehabilitation and recovery: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. Stroke 2016;47:e98–e169. doi: 10.1161/STR.0000000000000098.
164. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, *et al*. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med 2018;378:11–21. doi: 10.1056/NEJMoa1706442.
165. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, *et al*. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11–20. doi: 10.1056/NEJMoa1411587.
166. Bracard S, Ducrocq X, Mas JL, Soudant M, Oppenheim C, Moulin T, *et al*. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): A randomised controlled trial. Lancet Neurol 2016;15:1138–1147. doi: 10.1016/S1474-4422(16)30177-6.
167. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, *et al*. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 2015;372:1009–1018. doi: 10.1056/NEJMoa1414792.
168. Yang P, Song L, Zhang Y, Zhang X, Chen X, Li Y, *et al*. Intensive blood pressure control after endovascular thrombectomy for acute ischaemic stroke (ENCHANTED2/MT): A multicentre, open-label, blinded-endpoint, randomised controlled trial. Lancet 2022;400:1585–1596. doi: 10.1016/S0140-6736(22)01882-7.
169. Nam HS, Kim YD, Heo J, Lee H, Jung JW, Choi JK, *et al*. Intensive vs conventional blood pressure lowering after endovascular thrombectomy in acute ischemic stroke: The OPTIMAL-BP randomized clinical trial. JAMA 2023;330:832–842. doi: 10.1001/jama.2023.14590.
170. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, *et al*. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline from the American Heart Association/American Stroke Association. Stroke 2021;52:e364–e467. doi: 10.1161/STR.0000000000000375.
171. Robinson TG, Potter JF, Ford GA, Bulpitt CJ, Chernova J, Jagger C, *et al*. Effects of antihypertensive treatment after acute stroke in the Continue or Stop Post-Stroke Antihypertensives Collaborative Study (COSSACS): A prospective, randomised, open, blinded-endpoint trial. Lancet Neurol 2010;9:767–775. doi: 10.1016/S1474-4422(10)70163-0.
172. He J, Zhang Y, Xu T, Zhao Q, Wang D, Chen CS, *et al*. Effects of immediate blood pressure reduction on death and major disability in patients with acute ischemic stroke: The CATIS randomized clinical trial. JAMA 2014;311:479–489. doi: 10.1001/jama.2013.282543.
173. Kitagawa K, Yamamoto Y, Arima H, Maeda T, Sunami N, Kanzawa T, *et al*. Effect of standard vs intensive blood pressure control on the risk of recurrent stroke: A randomized clinical trial and meta-analysis. JAMA Neurol 2019;76:1309–1318. doi: 10.1001/jamaneurol.2019.2167.
174. Katsanos AH, Filippatou A, Manios E, Deftereos S, Parissis J, Frogoudaki A, *et al*. Blood pressure reduction and secondary stroke prevention: A systematic review and metaregression analysis of randomized clinical trials. Hypertension 2017;69:171–179. doi: 10.1161/HYPERTENSIONAHA.116.08485.
175. Wang L, Xu X, Zhang M, Hu C, Zhang X, Li C, *et al*. Prevalence of chronic kidney disease in China: Results from the sixth China chronic disease and risk factor surveillance. JAMA Intern Med 2023;183:298–310. doi: 10.1001/jamainternmed.2022.6817.
176. Zheng Y, Cai GY, Chen XM, Fu P, Chen JH, Ding XQ, *et al*. Prevalence, awareness, treatment, and control of hypertension in the non-dialysis chronic kidney disease patients. Chin Med J (Engl) 2013;126:2276–2280. doi: 10.3760/cma.j.issn.0366-6999.20130835.
177. Lv J, Ehteshami P, Sarnak MJ, Tighiouart H, Jun M, Ninomiya T, *et al*. Effects of intensive blood pressure lowering on the progression of chronic kidney disease: A systematic review and meta-analysis. CMAJ 2013;185:949–957. doi: 10.1503/cmaj.121468.
178. Upadhyay A, Earley A, Haynes SM, Uhlig K. Systematic review: Blood pressure target in chronic kidney disease and proteinuria as an effect modifier. Ann Intern Med 2011;154:541–548. doi: 10.7326/0003-4819-154-8-201104190-00335.
179. Beddhu S, Rocco MV, Toto R, Craven TE, Greene T, Bhatt U, *et al*. Effects of intensive systolic blood pressure control on kidney and cardiovascular outcomes in persons without kidney disease: A secondary analysis of a randomized trial. Ann Intern Med 2017;167:375–383. doi: 10.7326/M16-2966.
180. Tsai WC, Wu HY, Peng YS, Yang JY, Chen HY, Chiu YL, *et al*. Association of intensive blood pressure control and kidney disease progression in nondiabetic patients with chronic kidney disease: A systematic review and meta-analysis. JAMA Intern Med 2017;177:792–799. doi: 10.1001/jamainternmed.2017.0197.
181. Feldman RD, Liu L, Wu Z, Zhang Y, Yu X, Zhang XH. Hypertension attitude perspectives and needs (HAPPEN): A real-world survey of physicians and patients with hypertension in China. J Clin Hypertens (Greenwich) 2017;19:256–264. doi: 10.1111/jch.12912.
182. Martín-Fernández M, Vinyoles E, Real J, Soldevila N, Muñoz MÁ, Del-Val JL, *et al*. The prognostic value of blood pressure control delay in newly diagnosed hypertensive patients. J Hypertens 2019;37:426–431. doi: 10.1097/HJH.0000000000001896.
183. Zhang Y, Zhang X, Liu L, Zanchetti A. [OP.LB01.03] Benefits of early blood pressure control on cardiovascular outcomes: A subgroup analysis of the felodipine event reduction (fever) study. J Hypertens 2016;34:e36. doi: 10.1097/01.hjh.0000491427.85692.32.
184. Cheong AT, Mohd Said S, Muksan N. Time to achieve first blood pressure control after diagnosis among hypertensive patients at primary health care clinics: A preliminary study. Asia Pac J Public Health 2015;27:N485–N494. doi: 10.1177/1010539512472361.
185. Wang TD, Chiang CE, Chao TH, Cheng HM, Wu YW, Wu YJ, *et al*. 2022 guidelines of the Taiwan society of cardiology and the Taiwan Hypertension Society for the management of hypertension. Acta Cardiol Sin 2022;38:225–325. doi: 10.6515/ACS.202205_38(3)0.20220321A.
186. Wei J, Galaviz KI, Kowalski AJ, Magee MJ, Haw JS, Narayan KMV, *et al*. Comparison of cardiovascular events among users of different classes of antihypertension medications: A systematic review and network meta-analysis. JAMA Netw Open 2020;3:e1921618. doi: 10.1001/jamanetworkopen.2019.21618.
187. Wright JM, Musini VM, Gill R. First-line drugs for hypertension. Cochrane Database Syst Rev 2018;4:CD001841. doi: 10.1002/14651858.CD001841.pub3.
188. Zhu J, Chen N, Zhou M, Guo J, Zhu C, Zhou J, *et al*. Calcium channel blockers versus other classes of drugs for hyperten-

sion. Cochrane Database Syst Rev 2021;10:CD003654. doi: 10.1002/14651858.CD003654.pub5.
189. Reinhart M, Puil L, Salzwedel DM, Wright JM. First-line diuretics versus other classes of antihypertensive drugs for hypertension. Cochrane Database Syst Rev 2023;7:CD008161. doi: 10.1002/14651858.CD008161.pub3.
190. He T, Liu X, Li Y, Liu XY, Wu QY, Liu ML, *et al*. High-dose calcium channel blocker (CCB) monotherapy vs combination therapy of standard-dose CCBs and angiotensin receptor blockers for hypertension: A meta-analysis. J Hum Hypertens 2017;31:79–88. doi: 10.1038/jhh.2016.46.
191. Pongpanich P, Pitakpaiboonkul P, Takkavatakarn K, Praditpornsilpa K, Eiam-Ong S, Susantitaphong P. The benefits of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers combined with calcium channel blockers on metabolic, renal, and cardiovascular outcomes in hypertensive patients: A meta-analysis. Int Urol Nephrol 2018;50:2261–2278. doi: 10.1007/s11255-018-1991-x.
192. Weisser B, Predel HG, Gillessen A, Hacke C, Vor dem Esche J, Rippin G, *et al*. Single pill regimen leads to better adherence and clinical outcome in daily practice in patients suffering from hypertension and/or dyslipidemia: Results of a meta-analysis. High Blood Press Cardiovasc Prev 2020;27:157–164. doi: 10.1007/s40292-020-00370-5.
193. Parati G, Kjeldsen S, Coca A, Cushman WC, Wang J. Adherence to single-pill versus free-equivalent combination therapy in hypertension: A systematic review and meta-analysis. Hypertension 2021;77:692–705. doi: 10.1161/HYPERTENSIONAHA.120.15781.
194. Chi C, Tai C, Bai B, Yu S, Karamanou M, Wang J, *et al*. Angiotensin system blockade combined with calcium channel blockers is superior to other combinations in cardiovascular protection with similar blood pressure reduction: A meta-analysis in 20,451 hypertensive patients. J Clin Hypertens (Greenwich) 2016;18:801–808. doi: 10.1111/jch.12771.
195. Peeters LEJ, Kester MP, Feyz L, Van Den Bemt P, Koch BCP, Van Gelder T, *et al*. Pharmacokinetic and pharmacodynamic considerations in the treatment of the elderly patient with hypertension. Expert Opin Drug Metab Toxicol 2019;15:287–297. doi: 10.1080/17425255.2019.1588249.
196. Hypertension Branch of the Chinese Geriatrics Society, National Clinical Research Center for Geriatric Diseases, China Alliance for the Prevention and Treatment of Cardiovascular Diseases in the Elderly. Chinese guidelines for the management of hypertension in the elderly (in Chinese). Chin J Geriatrics Res (Electronic Edition) 2019;6:1–27.
197. Poole-Wilson PA, Lubsen J, Kirwan BA, van Dalen FJ, Wagener G, Danchin N, *et al*. Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with stable angina requiring treatment (ACTION trial): Randomized controlled trial. Lancet 2004;364:849–857. doi: 10.1016/S0140-6736(04)16980-8.
198. Rehnqvist N, Hjemdahl P, Billing E, Björkander I, Eriksson SV, Forslund L, *et al*. Effects of metoprolol vs verapamil in patients with stable angina pectoris. The Angina Prognosis Study in Stockholm (APSIS). Eur Heart J 1996;17:76–81. doi: 10.1093/oxfordjournals.eurheartj.a014695.
199. Ferrari R, Pavasini R, Camici PG, Crea F, Danchin N, Pinto F, *et al*. Anti-anginal drugs-beliefs and evidence: Systematic review covering 50 years of medical treatment. Eur Heart J 2019;40:190–194. doi: 10.1093/eurheartj/ehy504.
200. Safi S, Sethi NJ, Korang SK, Nielsen EE, Feinberg J, Gluud C, *et al*. Beta-blockers in patients without heart failure after myocardial infarction. Cochrane Database Syst Rev 2021;11:CD012565. doi: 10.1002/14651858.CD012565.pub2.
201. ONTARGET Investigators; Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, *et al*. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008;358:1547–1559. doi: 10.1056/NEJMoa0801317.
202. Lin LM, Wu Y, Wu MF, Lin JX. Focus on the novel cardiovascular drug LZC696: From evidence to clinical consideration. Cardiovasc Drugs Ther 2016;30:623–633. doi: 10.1007/s10557-016-6699-5.
203. Zheng C, Dai H, Huang J, Lin M, Zheng Q, Tang P, *et al*. The efficacy and safety of sacubitril/valsartan in the treatment of chronic heart failure: A meta-analysis. Am J Transl Res 2021;13:12114–12128.
204. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, *et al*. 2022 AHA/ACC/HFSA GUIDELINE for the Management of Heart Failure: Executive summary: A report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. Circulation 2022;145:e876–e894. doi: 10.1161/CIR.0000000000001062.
205. Solomon SD, Zile M, Pieske B, Voors A, Shah A, Kraigher-Krainer E, *et al*. The angiotensin receptor neprilysin inhibitor LCZ696 in heart failure with preserved ejection fraction: A phase 2 double-blind randomised controlled trial. Lancet 2012;380:1387–1395. doi: 10.1016/S0140-6736(12)61227-6.
206. McMurray JJV, Jackson AM, Lam CSP, Redfield MM, Anand IS, Ge J, *et al*. Effects of sacubitril-valsartan versus valsartan in women compared with men with heart failure and preserved ejection fraction: Insights from PARAGON-HF. Circulation 2020;141:338–351. doi: 10.1161/CIRCULATIONAHA.119.044491.
207. Solomon SD, McMurray JJV, Anand IS, Ge J, Lam CSP, Maggioni AP, *et al*. Angiotensin-neprilysin inhibition in heart failure with preserved ejection fraction. N Engl J Med 2019;381:1609–1620. doi: 10.1056/NEJMoa1908655.
208. Arima H, Chalmers J, Woodward M, Anderson C, Rodgers A, Davis S, *et al*. Lower target blood pressures are safe and effective for the prevention of recurrent stroke: The PROGRESS trial. J Hypertens 2006;24:1201–1208. doi: 10.1097/01.hjh.0000226212.34055.86.
209. Toschke AM, Gulliford MC, Wolfe CD, Rudd AG, Heuschmann PU. Antihypertensive treatment after first stroke in primary care: Results from the General Practitioner Research Database. J Hypertens 2011;29:154–160. doi: 10.1097/HJH.0b013e32833f3897.
210. Liu L, Wang Z, Gong L, Zhang Y, Thijs L, Staessen JA, *et al*. Blood pressure reduction for the secondary prevention of stroke: A Chinese trial and a systematic review of the literature. Hypertens Res 2009;32:1032–1040. doi: 10.1038/hr.2009.139.
211. Zonneveld TP, Richard E, Vergouwen MD, Nederkoorn PJ, de Haan R, Roos YB, *et al*. Blood pressure-lowering treatment for preventing recurrent stroke, major vascular events, and dementia in patients with a history of stroke or transient ischaemic attack. Cochrane Database Syst Rev 2018;7:CD007858. doi: 10.1002/14651858.CD007858.pub2.
212. Wang WT, You LK, Chiang CE, Sung SH, Chuang SY, Cheng HM, *et al*. Comparative effectiveness of blood pressure-lowering drugs in patients who have already suffered from stroke: Traditional and Bayesian network meta-analysis of randomized trials. Medicine (Baltimore) 2016;95:e3302. doi: 10.1097/MD.0000000000003302.
213. Feng A, Wang W, Du C, He M. A systematic review and meta-analysis of early diagnosis and treatment of hypertensive stroke under calcium channel blockers. Ann Palliat Med 2021;10:6715–6725. doi: 10.21037/apm-21-1272.
214. Wang G, Chen Y, Li L, Tang W, Wright JM. First-line renin-angiotensin system inhibitors vs. other first-line antihypertensive drug classes in hypertensive patients with type 2 diabetes mellitus. J Hum Hypertens 2018;32:494–506. doi: 10.1038/s41371-018-0066-x.
215. Filippatos TD, Tsimihodimos V, Elisaf MS. Mechanisms of blood pressure reduction with sodium-glucose co-transporter 2 (SGLT2) inhibitors. Expert Opin Pharmacother 2016;17:1581–1583. doi: 10.1080/14656566.2016.1201073.
216. Zhang YL, Zhou C, Li XF, Yang MN, Tao L, Zheng XY, *et al*. Beinaglutide showed significant weight-loss benefit and effective glycaemic control for the treatment of type 2 diabetes in a real-world setting: A 3-month, multicentre, observational, retrospective, open-label study. Obes Sci Pract 2019;5:366–375. doi: 10.1002/osp4.342.
217. McGuire DK, Shih WJ, Cosentino F, Charbonnel B, Cherney DZI, Dagogo-Jack S, *et al*. Association of SGLT2 inhibitors with cardiovascular and kidney outcomes in patients with type 2 diabetes: A meta-analysis. JAMA Cardiol 2021;6:148–158. doi: 10.1001/jamacardio.2020.4511.
218. Palmer SC, Tendal B, Mustafa RA, Vandvik PO, Li S, Hao Q, *et al*. Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: Systematic review and network meta-analysis of randomised controlled trials. BMJ 2021;372:m4573. doi: 10.1136/bmj.m4573.
219. Kristensen SL, Rørth R, Jhund PS, Docherty KF, Sattar N, Preiss D, *et al*. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: A sys-

tematic review and meta-analysis of cardiovascular outcome trials. Lancet Diabetes Endocrinol 2019;7:776–785. doi: 10.1016/S2213-8587(19)30249-9.
220. O'Meara E, McDonald M, Chan M, Ducharme A, Ezekowitz JA, Giannetti N, *et al*. CCS/CHFS heart failure guidelines: Clinical trial update on functional mitral regurgitation, SGLT2 inhibitors, ARNI in HFpEF, and Tafamidis in amyloidosis. Can J Cardiol 2020;36:159–169. doi: 10.1016/j.cjca.2019.11.036.
221. Mishima E, Haruna Y, Arima H. Renin-angiotensin system inhibitors in hypertensive adults with non-diabetic CKD with or without proteinuria: A systematic review and meta-analysis of randomized trials. Hypertens Res 2019;42:469–482. doi: 10.1038/s41440-018-0116-3.
222. Strippoli GF, Bonifati C, Craig M, Navaneethan SD, Craig JC. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists for preventing the progression of diabetic kidney disease. Cochrane Database Syst Rev 2006;2006:CD006257. doi: 10.1002/14651858.CD006257.
223. Shi ZW. Current status of aspirin use for prevention of cardiovascular disease (in Chinese). Chin J Digest 2020;40:292–295.
224. Zhang YX, Gao HC, Zhang CR, Sun MS, Chen YJ, Zeng LS, *et al*. Advances in the study of structural modification of aspirin and their biological activities (in Chinese). Chin J Org Chem 2020;40:300–326. doi: 10.6023/cjoc2019070.
225. Sugawara M, Goto Y, Yamazaki T, Teramoto T, Oikawa S, Shimada K, *et al*. Low-dose aspirin for primary prevention of cardiovascular events in elderly Japanese patients with atherosclerotic risk factors: Subanalysis of a randomized clinical trial (JPPP-70). Am J Cardiovasc Drugs 2019;19:299–311. doi: 10.1007/s40256-018-0313-0.
226. Shah SN, Munjal YP, Kamath SA, Wander GS, Mehta N, Mukherjee S, *et al*. Indian guidelines on hypertension-IV (2019). J Hum Hypertens 2020;34:745–758. doi: 10.1038/s41371-020-0349-x.
227. Bibbins-Domingo K, Force USPST. Aspirin use for the primary prevention of cardiovascular disease and colorectal cancer: U.S. preventive services task force recommendation statement. Ann Intern Med 2016;164:836–845. doi: 10.7326/M16-0577.
228. The Writing Group of 2019 Chinese Expert Consensus on Aspirin in Primary Prevention of Cardiovascular Disease. Chinese expert consensus on the use of aspirin in the primary prevention of cardiovascular disease (in Chinese). Chin Video J Cardiol 2019;02:1–5. doi: 10.3760/cma.j.issn.2096-1588.2019.1000020.
229. ASCEND Study Collaborative Group; Bowman L, Mafham M, Wallendszus K, Stevens W, Buck G, *et al*. Effects of aspirin for primary prevention in persons with diabetes mellitus. N Engl J Med 2018;379:1529–1539. doi: 10.1056/NEJMoa1804988.
230. Zheng SL, Roddick AJ. Association of aspirin use for primary prevention with cardiovascular events and bleeding events: A systematic review and meta-analysis. JAMA 2019;321:277–287. doi: 10.1001/jama.2018.20578.
231. Calderone D, Greco A, Ingala S, Agnello F, Franchina G, Scalia L, *et al*. Efficacy and safety of aspirin for primary cardiovascular risk prevention in younger and older age: An updated systematic review and meta-analysis of 173,810 subjects from 21 randomized studies. Thromb Haemost 2022;122:445–455. doi: 10.1055/a-1667-7427.
232. US Preventive Services Task Force; Davidson KW, Barry MJ, Mangione CM, Cabana M, Chelmow D, *et al*. Aspirin use to prevent cardiovascular disease: US preventive services task force recommendation statement. JAMA 2022;327:1577–1584. doi: 10.1001/jama.2022.4983.
233. Chen C, Zhu XY, Li D, Lin Q, Zhou K. Clinical efficacy and safety of spironolactone in patients with resistant hypertension: A systematic review and meta-analysis. Medicine (Baltimore) 2020;99:e21694. doi: 10.1097/MD.0000000000021694.
234. Lauder L, Azizi M, Kirtane AJ, Bohm M, Mahfoud F. Device-based therapies for arterial hypertension. Nat Rev Cardiol 2020;17:614–628. doi: 10.1038/s41569-020-0364-1.
235. Townsend RR, Mahfoud F, Kandzari DE, Kario K, Pocock S, Weber MA, *et al*. Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): A randomised, sham-controlled, proof-of-concept trial. Lancet 2017;390:2160–2170. doi: 10.1016/S0140-6736(17)32281-X.
236. Kandzari DE, Böhm M, Mahfoud F, Townsend RR, Weber MA, Pocock S, *et al*. Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial. Lancet 2018;391:2346–2355. doi: 10.1016/S0140-6736(18)30951-6.
237. Mahfoud F, Böhm M, Schmieder R, Narkiewicz K, Ewen S, Ruilope L, *et al*. Effects of renal denervation on kidney function and long-term outcomes: 3-year follow-up from the Global SYMPLICITY Registry. Eur Heart J 2019;40:3474–3482. doi: 10.1093/eurheartj/ehz118.
238. Mahfoud F, Kandzari DE, Kario K, Townsend RR, Weber MA, Schmieder RE, *et al*. Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs (SPYRAL HTN-ON MED): A randomised, sham-controlled trial. Lancet 2022;399:1401–1410. doi: 10.1016/S0140-6736(22)00455-X.
239. Kario K, Kim BK, Aoki J, Wong AY, Lee YH, Wongpraparut N, *et al*. Renal denervation in Asia: Consensus statement of the Asia renal denervation consortium. Hypertension 2020;75:590–602. doi: 10.1161/HYPERTENSIONAHA.119.13671.
240. Ahmad Y, Kane C, Arnold AD, Cook CM, Keene D, Shun-Shin M, *et al*. Randomized blinded placebo-controlled trials of renal sympathetic denervation for hypertension: A meta-analysis. Cardiovasc Revasc Med 2022;34:112–118. doi: 10.1016/j.carrev.2021.01.031.
241. Sardar P, Bhatt DL, Kirtane AJ, Kennedy KF, Chatterjee S, Giri J, *et al*. Sham-controlled randomized trials of catheter-based renal denervation in patients with hypertension. J Am Coll Cardiol 2019;73:1633–1642. doi: 10.1016/j.jacc.2018.12.082.
242. Schmieder RE, Hogerl K, Jung S, Bramlage P, Veelken R, Ott C. Patient preference for therapies in hypertension: A cross-sectional survey of German patients. Clin Res Cardiol 2019;108:1331–1342. doi: 10.1007/s00392-019-01468-0.
243. Verdecchia P, Reboldi G, Angeli F. The 2020 International Society of Hypertension global hypertension practice guidelines–key messages and clinical considerations. Eur J Intern Med 2020;82:1–6. doi: 10.1016/j.ejim.2020.09.001.
244. van den Born BH, Lip GYH, Brguljan-Hitij J, Cremer A, Segura J, Morales E, *et al*. ESC Council on hypertension position document on the management of hypertensive emergencies. Eur Heart J Cardiovasc Pharmacother 2019;5:37–46. doi: 10.1093/ehjcvp/pvy032.
245. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr., *et al*. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 report. JAMA 2003;289:2560–2572. doi: 10.1001/jama.289.19.2560.
246. Kim K, Kim JY, Choi EY, Kwon HM, Rim SJ. Prevalence and risk factors for secondary hypertension among young Korean men. Rev Cardiovasc Med 2020;21:627–634. doi: 10.31083/j.rcm.2020.04.121.
247. Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, *et al*. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J 2014;35:2873–2926. doi: 10.1093/eurheartj/ehu281.
248. Mokashi SA, Svensson LG. Guidelines for the management of thoracic aortic disease in 2017. Gen Thorac Cardiovasc Surg 2019;67:59–65. doi: 10.1007/s11748-017-0831-8.
249. Daugherty SL, Powers JD, Magid DJ, Tavel HM, Masoudi FA, Margolis KL, *et al*. Incidence and prognosis of resistant hypertension in hypertensive patients. Circulation 2012;125:1635–1642. doi: 10.1161/CIRCULATIONAHA.111.068064.
250. Noubiap JJ, Nansseu JR, Nyaga UF, Sime PS, Francis I, Bigna JJ. Global prevalence of resistant hypertension: A meta-analysis of data from 3.2 million patients. Heart 2019;105:98–105. doi: 10.1136/heartjnl-2018-313599.
251. van der Sande NGC, de Beus E, Bots ML, Voskuil M, Blankestijn PJ, Visseren F, *et al*. Apparent resistant hypertension and the risk of vascular events and mortality in patients with manifest vascular disease. J Hypertens 2018;36:143–150. doi: 10.1097/HJH.0000000000001494.
252. Käyser SC, Dekkers T, Groenewoud HJ, van der Wilt GJ, Carel Bakx J, van der Wel MC, *et al*. Study heterogeneity and estimation of prevalence of primary aldosteronism: A systematic review and meta-regression analysis. J Clin Endocrinol Metab 2016;101:2826–2835. doi: 10.1210/jc.2016-1472.
253. Hundemer GL, Curhan GC, Yozamp N, Wang M, Vaidya A. Cardiometabolic outcomes and mortality in medically treated primary aldosteronism: A retrospective cohort study. Lancet Dia-

betes Endocrinol 2018;6:51–59. doi: 10.1016/S2213-8587(17)30367-4.
254. Monticone S, D'Ascenzo F, Moretti C, Williams TA, Veglio F, Gaita F, *et al*. Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: A systematic review and meta-analysis. Lancet Diabetes Endocrinol 2018;6:41–50. doi: 10.1016/S2213-8587(17)30319-4.
255. Mulatero P, Monticone S, Deinum J, Amar L, Prejbisz A, Zennaro MC, *et al*. Genetics, prevalence, screening and confirmation of primary aldosteronism: A position statement and consensus of the Working Group on Endocrine Hypertension of The European Society of Hypertension. J Hypertens 2020;38:1919–1928. doi: 10.1097/HJH.0000000000002510.
256. Funder JW, Carey RM, Mantero F, Murad MH, Reincke M, Shibata H, *et al*. The management of primary aldosteronism: Case detection, diagnosis, and treatment: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2016;101:1889–1916. doi: 10.1210/jc.2015-4061.
257. Naruse M, Katabami T, Shibata H, Sone M, Takahashi K, Tanabe A, *et al*. Japan Endocrine Society clinical practice guideline for the diagnosis and management of primary aldosteronism 2021. Endocr J 2022;69:327–359. doi: 10.1507/endocrj.EJ21-0508.
258. Hundemer GL, Imsirovic H, Vaidya A, Yozamp N, Goupil R, Madore F, *et al*. Screening rates for primary aldosteronism among individuals with hypertension plus hypokalemia: A population-based retrospective cohort study. Hypertension 2022;79:178–186. doi: 10.1161/HYPERTENSIONAHA.121.18118.
259. Brown JM, Siddiqui M, Calhoun DA, Carey RM, Hopkins PN, Williams GH, *et al*. The unrecognized prevalence of primary aldosteronism: A cross-sectional study. Ann Intern Med 2020;173:10–20. doi: 10.7326/M20-0065.
260. Gkaniatsa E, Ekerstad E, Gavric M, Muth A, Trimpou P, Olsson DS, *et al*. Increasing incidence of primary aldosteronism in western Sweden during 3 decades–Yet an underdiagnosed disorder. J Clin Endocrinol Metab 2021;106:e3603–e3610. doi: 10.1210/clinem/dgab327.
261. Li N, Huang J, Zheng B, Cai H, Liu M, Liu L. Cost-effectiveness analysis of screening for primary aldosteronism in China. Clin Endocrinol (Oxf) 2021;95:414–422. doi: 10.1111/cen.14478.
262. Sato M, Morimoto R, Seiji K, Iwakura Y, Ono Y, Kudo M, *et al*. Cost-effectiveness analysis of the diagnosis and treatment of primary aldosteronism in Japan. Horm Metab Res 2015;47:826–832. doi: 10.1055/s-0035-1559645.
263. Xu Z, Yang J, Hu J, Song Y, He W, Luo T, *et al*. Primary aldosteronism in patients in china with recently detected hypertension. J Am Coll Cardiol 2020;75:1913–1922. doi: 10.1016/j.jacc.2020.02.052.
264. Kline GA, Prebtani APH, Leung AA, Schiffrin EL. Primary aldosteronism: A common cause of resistant hypertension. CMAJ 2017;189:E773–E778. doi: 10.1503/cmaj.161486.
265. Monticone S, Burrello J, Tizzani D, Bertello C, Viola A, Buffolo F, *et al*. Prevalence and clinical manifestations of primary aldosteronism encountered in primary care practice. J Am Coll Cardiol 2017;69:1811–1820. doi: 10.1016/j.jacc.2017.01.052.
266. Rossi GP, Bernini G, Caliumi C, Desideri G, Fabris B, Ferri C, *et al*. A prospective study of the prevalence of primary aldosteronism in 1,125 hypertensive patients. J Am Coll Cardiol 2006;48:2293–2300. doi: 10.1016/j.jacc.2006.07.059.
267. Wang K, Hu J, Yang J, Song Y, Fuller PJ, Hashimura H, *et al*. Development and validation of criteria for sparing confirmatory tests in diagnosing primary aldosteronism. J Clin Endocrinol Metab 2020;105:dgaa282. doi: 10.1210/clinem/dgaa282.
268. Liu X, Hao S, Bian J, Lou Y, Zhang H, Wu H, *et al*. Performance of aldosterone-to-renin ratio before washout of antihypertensive drugs in screening of primary aldosteronism. J Clin Endocrinol Metab 2024:dgae094. doi: 10.1210/clinem/dgae094.
269. Rossi GP, Ceolotto G, Rossitto G, Seccia TM, Maiolino G, Berton C, *et al*. Prospective validation of an automated chemiluminescence-based assay of renin and aldosterone for the work-up of arterial hypertension. Clin Chem Lab Med 2016;54:1441–1450. doi: 10.1515/cclm-2015-1094.
270. Ma L, Song Y, Mei M, He W, Hu J, Cheng Q, *et al*. Age-related cutoffs of plasma aldosterone/renin concentration for primary aldosteronism screening. Int J Endocrinol 2018;2018:8647026. doi: 10.1155/2018/8647026.
271. Tiu SC, Choi CH, Shek CC, Ng YW, Chan FK, Ng CM, *et al*. The use of aldosterone-renin ratio as a diagnostic test for primary hyperaldosteronism and its test characteristics under different conditions of blood sampling. J Clin Endocrinol Metab 2005;90:72–78. doi: 10.1210/jc.2004-1149.
272. Thuzar M, Young K, Ahmed AH, Ward G, Wolley M, Guo Z, *et al*. Diagnosis of primary aldosteronism by seated saline suppression test-variability between immunoassay and HPLC-MS/MS. J Clin Endocrinol Metab 2020;105:dgz150. doi: 10.1210/clinem/dgz150.
273. Endocrinology Branch of the Chinese Medical Association. Expert consensus on the diagnosis and treatment of primary aldosteronism (in Chinese). Chin J Endocrinol Metab 2020;36:727–736.
274. Zhen FF, Song Y, Yang SM, Hu JB, He WW, Wang ZH, *et al*. Comparison of the consistency of different methods for measuring plasma aldosterone concentration. Chin J Endocrinol Metab 2019;35:934–938.
275. Xiang Q, Wang W, Chen T, Yu K, Li Q, Zhang T, *et al*. The value of the post-captopril aldosterone/renin ratio for the diagnosis of primary aldosteronism and the influential factors: A meta-analysis. J Renin Angiotensin Aldosterone Syst 2020;21:1470320320972032. doi: 10.1177/1470320320972032.
276. Wu S, Yang J, Hu J, Song Y, He W, Yang S, *et al*. Confirmatory tests for the diagnosis of primary aldosteronism: A systematic review and meta-analysis. Clin Endocrinol (Oxf) 2019;90:641–648. doi: 10.1111/cen.13943.
277. Stowasser M, Ahmed AH, Cowley D, Wolley M, Guo Z, McWhinney BC, *et al*. Comparison of seated with recumbent saline suppression testing for the diagnosis of primary aldosteronism. J Clin Endocrinol Metab 2018;103:4113–4124. doi: 10.1210/jc.2018-01394.
278. Liu B, Hu J, Song Y, He W, Cheng Q, Wang Z, *et al*. Seated saline suppression test is comparable with captopril challenge test for the diagnosis of primary aldosteronism: A prospective study. Endocr Pract 2021;27:326–333. doi: 10.1016/j.eprac.2020.10.016.
279. Song Y, Yang S, He W, Hu J, Cheng Q, Wang Y, *et al*. Confirmatory tests for the diagnosis of primary aldosteronism: A prospective diagnostic accuracy study. Hypertension 2018;71:118–124. doi: 10.1161/HYPERTENSIONAHA.117.10197.
280. Luo YHW, Chen QF, Yang SM, Du ZP, Mei W, *et al*. Re-evaluation of the value of the captopril test in the diagnosis of primary aldosteronism and its appropriate cut-off points (in Chinese). Chin J Intern Med 2022;61:60–65.
281. Jaffe G, Gray Z, Krishnan G, Stedman M, Zheng Y, Han J, *et al*. Screening rates for primary aldosteronism in resistant hypertension: A cohort study. Hypertension 2020;75:650–659. doi: 10.1161/HYPERTENSIONAHA.119.14359.
282. Conroy PC, Hernandez S, Graves CE, Menut KC, Pearlstein S, Liu C, *et al*. Screening for primary aldosteronism is underutilized in patients with obstructive sleep apnea. Am J Med 2022;135:60–66. doi: 10.1016/j.amjmed.2021.07.041.
283. Li X, Liang J, Hu J, Ma L, Yang J, Zhang A, *et al*. Screening for primary aldosteronism on and off interfering medications. Endocrine 2024;83:178–187. doi: 10.1007/s12020-023-03520-6.
284. Liu X, Hao S, Bian J, Lou Y, Zhang H, Wu H, *et al*. Performance of aldosterone-to-renin ratio before washout of antihypertensive drugs in screening of primary aldosteronism. J Clin Endocrinol Metabol 2024:dgae094. doi: 10.1210/clinem/dgae094.
285. Nieman LK, Biller BM, Findling JW, Newell-Price J, Savage MO, Stewart PM, *et al*. The diagnosis of Cushing's syndrome: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2008;93:1526–1540. doi: 10.1210/jc.2008-0125.
286. Zheng X, Wang H, Zhang W, Feng S, Liu Y, Li S, *et al*. Diagnosis, manifestations, laboratory investigations, and prognosis in pediatric and adult Cushing's disease in a large center in China. Front Endocrinol (Lausanne) 2021;12:749246. doi: 10.3389/fendo.2021.749246.
287. Hakami OA, Ahmed S, Karavitaki N. Epidemiology and mortality of Cushing's syndrome. Best Pract Res Clin Endocrinol Metab 2021;35:101521. doi: 10.1016/j.beem.2021.101521.
288. Shimon I. Screening for Cushing's syndrome: Is it worthwhile? Pituitary 2015;18:201–205. doi: 10.1007/s11102-015-0634-9.
289. Kebebew E. Adrenal incidentaloma. N Engl J Med 2021;384:1542–1551. doi: 10.1056/NEJMcp2031112.
290. Aresta C, Soranna D, Giovanelli L, Favero V, Parazzoli C, Gennari L, *et al*. When to suspect hidden hypercortisolism in type 2 diabetes: A meta-analysis. Endocr Pract 2021;27:1216–1224. doi: 10.1016/j.eprac.2021.07.014.

291. Fleseriu M, Auchus R, Bancos I, Ben-Shlomo A, Bertherat J, Biermasz NR, *et al*. Consensus on diagnosis and management of Cushing's disease: A guideline update. Lancet Diabetes Endocrinol 2021;9:847–875. doi: 10.1016/S2213-8587(21)00235-7.
292. Galm BP, Qiao N, Klibanski A, Biller BMK, Tritos NA. Accuracy of laboratory tests for the diagnosis of Cushing syndrome. J Clin Endocrinol Metab 2020;105:dgaa105. doi: 10.1210/clinem/dgaa105.
293. Chinese Society of Endocrinology. Expert consensus on the diagnosis and treatment of primary aldosteronism (in Chinese). Chin J Endocrinol Metab 2020;36:727–736.
294. Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, Murad MH, *et al*. Pheochromocytoma and paraganglioma: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2014;99:1915–1942. doi: 10.1210/jc.2014-1498.
295. Shah MH, Goldner WS, Benson AB, Bergsland E, Blaszkowsky LS, Brock P, *et al*. Neuroendocrine and adrenal tumors, version 2.2021, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2021;19:839–868. doi: 10.6004/jnccn.2021.0032.
296. Kumar A, Pappachan JM, Fernandez CJ. Catecholamine-induced cardiomyopathy: An endocrinologist's perspective. Rev Cardiovasc Med 2021;22:1215–1228. doi: 10.31083/j.rcm2204130.
297. Santos JRU, Brofferio A, Viana B, Pacak K. Catecholamine-induced cardiomyopathy in pheochromocytoma: How to manage a rare complication in a rare disease? Horm Metab Res 2019;51:458–469. doi: 10.1055/a-0669-9556.
298. Hu JT, Dai YL, Wei C, *et al*. A retrospective study of 119 patients with pheochromocytoma (in Chinese). Chin J Hemorheology 2021;31:183–186.
299. Liu QX, Zhou WY, Zhang CB. Current status of catecholamine and its metabolite detection and expectations for standardization (in Chinese). Chin J Lab Med 2020;43:322–327.
300. Rao D, Peitzsch M, Prejbisz A, Hanus K, Fassnacht M, Beuschlein F, *et al*. Plasma methoxytyramine: Clinical utility with metanephrines for diagnosis of pheochromocytoma and paraganglioma. Eur J Endocrinol 2017;177:103–113. doi: 10.1530/EJE-17-0077.
301. Chen Y, Xiao H, Zhou X, Huang X, Li Y, Xiao H, *et al*. Accuracy of plasma free metanephrines in the diagnosis of pheochromocytoma and paraganglioma: A systematic review and meta-analysis. Endocr Pract 2017;23:1169–1177. doi: 10.4158/EP171877.OR.
302. Woo S, Suh CH, Kim SY, Cho JY, Kim SH. Pheochromocytoma as a frequent false-positive in adrenal washout CT: A systematic review and meta-analysis. Eur Radiol 2018;28:1027–1036. doi: 10.1007/s00330-017-5076-5.
303. Han S, Suh CH, Woo S, Kim YJ, Lee JJ. Performance of ^{68}Ga-DOTA-conjugated somatostatin receptor-targeting peptide PET in detection of pheochromocytoma and paraganglioma: A systematic review and metaanalysis. J Nucl Med 2019;60:369–376. doi: 10.2967/jnumed.118.211706.
304. Kan Y, Zhang S, Wang W, Liu J, Yang J, Wang Z. 68Ga-somatostatin receptor analogs and ^{18}F-FDG PET/CT in the localization of metastatic pheochromocytomas and paragangliomas with germline mutations: A meta-analysis. Acta Radiol 2018;59:1466–1474. doi: 10.1177/0284185118764206.
305. Singh D, Shukla J, Walia R, Vatsa R, Paul N, Chhabra A, *et al*. Role of [68Ga]DOTANOC PET/computed tomography and [131I]MIBG scintigraphy in the management of patients with pheochromocytoma and paraganglioma: A prospective study. Nucl Med Commun 2020;41:1047–1059. doi: 10.1097/MNM.0000000000001251.
306. Buffet A, Burnichon N, Favier J, Gimenez-Roqueplo AP. An overview of 20 years of genetic studies in pheochromocytoma and paraganglioma. Best Pract Res Clin Endocrinol Metab 2020;34:101416. doi: 10.1016/j.beem.2020.101416.
307. Crona J, Lamarca A, Ghosal S, Welin S, Skogseid B, Pacak K. Genotype-phenotype correlations in pheochromocytoma and paraganglioma: A systematic review and individual patient meta-analysis. Endocr Relat Cancer 2019;26:539–550. doi: 10.1530/ERC-19-0024.
308. Yonamine M, Wasano K, Aita Y, Sugasawa T, Takahashi K, Kawakami Y, *et al*. Prevalence of germline variants in a large cohort of Japanese patients with pheochromocytoma and/or paraganglioma. Cancers (Basel) 2021;13:4014. doi: 10.3390/cancers13164014.
309. Peng M, Jiang XJ, Dong H, Zou YB, Zhang HM, Song L, *et al*. Etiology of renal artery stenosis in 2047 patients: A single-center retrospective analysis during a 15-year period in China. J Hum Hypertens 2016;30:124–128. doi: 10.1038/jhh.2015.40.
310. Rimoldi SF, Scherrer U, Messerli FH. Secondary arterial hypertension: When, who, and how to screen? Eur Heart J 2014;35:1245–1254. doi: 10.1093/eurheartj/eht534.
311. de Mast Q, Beutler JJ. The prevalence of atherosclerotic renal artery stenosis in risk groups: A systematic literature review. J Hypertens 2009;27:1333–1340. doi: 10.1097/HJH.0b013e328329bbf4.
312. Song JJ, Liu XN, Cai J, Ma WJ, Song L, Zhang HM, *et al*. Analysis of clinical characteristics in young hypertensive patients (in Chinese). Chin Gen Pract 2019;22:3850–3856.
313. van Jaarsveld BC, Krijnen P, Derkx FH, Deinum J, Woittiez AJ, Postma CT, *et al*. Resistance to antihypertensive medication as predictor of renal artery stenosis: Comparison of two drug regimens. J Hum Hypertens 2001;15:669–676. doi: 10.1038/sj.jhh.1001258.
314. Evans KL, Tuttle KR, Folt DA, Dawson T, Haller ST, Brewster PS, *et al*. Use of renin-angiotensin inhibitors in people with renal artery stenosis. Clin J Am Soc Nephrol 2014;9:1199–1206. doi: 10.2215/CJN.11611113.
315. Ghaffari S, Sohrabi B, Siahdasht RB, Pourafkari L. Prevalence and predictors of renal artery stenosis in hypertensive patients undergoing coronary angiography. Hypertens Res 2009;32:1009–1014. doi: 10.1038/hr.2009.149.
316. Drafting Group of the Expert Consensus of the Hypertension Branch of the China International Exchange and Promotion Association for Medical and Healthcare. Chinese expert consensus on the diagnosis and management of renal artery stenosis (in Chinese). Chin Circ J 2017;32:835–844.
317. Vasbinder GB, Nelemans PJ, Kessels AG, Kroon AA, de Leeuw PW, van Engelshoven JM. Diagnostic tests for renal artery stenosis in patients suspected of having renovascular hypertension: A meta-analysis. Ann Intern Med 2001;135:401–411. doi: 10.7326/0003-4819-135-6-200109180-00009.
318. Wang L, Zhu L, Li G, Zhang Y, Jiang Y, Shui B, *et al*. Gadolinium-enhanced magnetic resonance versus computed tomography angiography for renal artery stenosis: A systematic review and meta-analysis. J Formos Med Assoc 2021;120:1171–1178. doi: 10.1016/j.jfma.2021.01.007.
319. Tan KT, van Beek EJ, Brown PW, van Delden OM, Tijssen J, Ramsay LE. Magnetic resonance angiography for the diagnosis of renal artery stenosis: A meta-analysis. Clin Radiol 2002;57:617–624. doi: 10.1053/crad.2002.0941.
320. Williams GJ, Macaskill P, Chan SF, Karplus TE, Yung W, Hodson EM, *et al*. Comparative accuracy of renal duplex sonographic parameters in the diagnosis of renal artery stenosis: Paired and unpaired analysis. AJR Am J Roentgenol 2007;188:798–811. doi: 10.2214/AJR.06.0355.
321. Vasbinder GB, Nelemans PJ, Kessels AG, Kroon AA, Maki JH, Leiner T, *et al*. Accuracy of computed tomographic angiography and magnetic resonance angiography for diagnosing renal artery stenosis. Ann Intern Med 2004;141:674–682; discussion 682. doi: 10.7326/0003-4819-141-9-200411020-00007.
322. Taylor A. Functional testing: ACEI renography. Semin Nephrol 2000;20:437–444.
323. Hackam DG, Duong-Hua ML, Mamdani M, Li P, Tobe SW, Spence JD, *et al*. Angiotensin inhibition in renovascular disease: A population-based cohort study. Am Heart J 2008;156:549–555. doi: 10.1016/j.ahj.2008.05.013.
324. Losito A, Errico R, Santirosi P, Lupattelli T, Scalera GB, Lupattelli L. Long-term follow-up of atherosclerotic renovascular disease. Beneficial effect of ACE inhibition. Nephrol Dial Transplant 2005;20:1604–1609. doi: 10.1093/ndt/gfh865.
325. Sofroniadou S, Kassimatis T, Srirajaskanthan R, Reidy J, Goldsmith D. Long-term safety and efficacy of renin-angiotensin blockade in atherosclerotic renal artery stenosis. Int Urol Nephrol 2012;44:1451–1459. doi: 10.1007/s11255-011-0091-y.
326. van de Ven PJ, Beutler JJ, Kaatee R, Beek FJ, Mali WP, Koomans HA. Angiotensin converting enzyme inhibitor-induced renal dysfunction in atherosclerotic renovascular disease. Kidney Int 1998;53:986–993. doi: 10.1111/j.1523-1755.1998.00840.x.
327. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, *et al*. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries Endorsed by: The European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the

European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J 2018;39:763–816. doi: 10.1093/eurheartj/ehx095.
328. Mount P, Kumar SK, MacGinley R, Mantha M, Roberts M, Mangos G, *et al*. The CARI guidelines. Inhibition of the renin-angiotensin system. Nephrology (Carlton) 2010;15(Suppl 1):S234–S243. doi: 10.1111/j.1440-1797.2009.01246.x.
329. Rabi DM, Daskalopoulou SS, Padwal RS, Khan NA, Grover SA, Hackam DG, *et al*. The 2011 Canadian Hypertension Education Program recommendations for the management of hypertension: Blood pressure measurement, diagnosis, assessment of risk, and therapy. Can J Cardiol 2011;27:e411–e412. doi: 10.1016/j.cjca.2011.03.015.
330. Chrysochou C, Foley RN, Young JF, Khavandi K, Cheung CM, Kalra PA. Dispelling the myth: The use of renin-angiotensin blockade in atheromatous renovascular disease. Nephrol Dial Transplant 2012;27:1403–1409. doi: 10.1093/ndt/gfr496.
331. Spence JD. Treatment options for renovascular hypertension. Expert Opin Pharmacother 2002;3:411–416. doi: 10.1517/14656566.3.4.411.
332. Jenks S, Yeoh SE, Conway BR. Balloon angioplasty, with and without stenting, versus medical therapy for hypertensive patients with renal artery stenosis. Cochrane Database Syst Rev 2014;2014:CD002944. doi: 10.1002/14651858.CD002944.pub2.
333. Khosla S, Ahmed A, Siddiqui M, Trivedi A, Benatar D, Salem Y, *et al*. Safety of angiotensin-converting enzyme inhibitors in patients with bilateral renal artery stenosis following successful renal artery stent revascularization. Am J Ther 2006;13:306–308. doi: 10.1097/00045391-200607000-00005.
334. Safian RD, Textor SC. Renal-artery stenosis. N Engl J Med 2001;344:431–442. doi: 10.1056/NEJM200102083440607.
335. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, *et al*. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): A collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. Circulation 2006;113:e463–e654. doi: 10.1161/CIRCULATIONAHA.106.174526.
336. Chen Y, Pan H, Luo G, Li P, Dai X. Use of percutaneous transluminal renal angioplasty in atherosclerotic renal artery stenosis: A systematic review and meta-analysis. J Int Med Res 2021;49:300060520983585. doi: 10.1177/0300060520983585.
337. Bhalla V, Textor SC, Beckman JA, Casanegra AI, Cooper CJ, Kim ESH, *et al*. Revascularization for renovascular disease: A scientific statement from the American Heart Association. Hypertension 2022;79:e128–e143. doi: 10.1161/HYP.0000000000000217.
338. Green D, Ritchie JP, Chrysochou C, Kalra PA. Revascularization of atherosclerotic renal artery stenosis for chronic heart failure versus acute pulmonary oedema. Nephrology (Carlton) 2018;23:411–417. doi: 10.1111/nep.13038.
339. Ritchie J, Green D, Chrysochou C, Chalmers N, Foley RN, Kalra PA. High-risk clinical presentations in atherosclerotic renovascular disease: Prognosis and response to renal artery revascularization. Am J Kidney Dis 2014;63:186–197. doi: 10.1053/j.ajkd.2013.07.020.
340. van den Berg DT, Deinum J, Postma CT, van der Wilt GJ, Riksen NP. The efficacy of renal angioplasty in patients with renal artery stenosis and flash oedema or congestive heart failure: A systematic review. Eur J Heart Fail 2012;14:773–781. doi: 10.1093/eurjhf/hfs037.
341. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, *et al*. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med 2017;13:479–504. doi: 10.5664/jcsm.6506.
342. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of adult obstructive sleep apnea with positive airway pressure: An American Academy of Sleep Medicine Systematic Review, Meta-Analysis, and GRADE Assessment. J Clin Sleep Med 2019;15:301–334. doi: 10.5664/jcsm.7638.
343. Akashiba T, Inoue Y, Uchimura N, Ohi M, Kasai T, Kawana F, *et al*. Sleep apnea syndrome (SAS) clinical practice guidelines 2020. Respir Investig 2022;60:3–32. doi: 10.1016/j.resinv.2021.08.010.
344. Shang W, Zhang Y, Liu L, Chen F, Wang G, Han D. Benefits of continuous positive airway pressure on blood pressure in patients with hypertension and obstructive sleep apnea: A meta-analysis. Hypertens Res 2022;45:1802–1813. doi: 10.1038/s41440-022-00954-9.
345. Labarca G, Dreyse J, Drake L, Jorquera J, Barbe F. Efficacy of continuous positive airway pressure (CPAP) in the prevention of cardiovascular events in patients with obstructive sleep apnea: Systematic review and meta-analysis. Sleep Med Rev 2020;52:101312. doi: 10.1016/j.smrv.2020.101312.
346. Sánchez-de-la-Torre M, Gracia-Lavedan E, Benitez ID, Sánchez-de-la-Torre A, Moncusí-Moix A, Torres G, *et al*. Adherence to CPAP treatment and the risk of recurrent cardiovascular events: A meta-analysis. JAMA 2023;330:1255–1265. doi: 10.1001/jama.2023.17465.
347. Wang Y, Li CX, Lin YN, Zhang LY, Li SQ, Zhang L, *et al*. The role of aldosterone in OSA and OSA-related hypertension. Front Endocrinol (Lausanne) 2021;12:801689. doi: 10.3389/fendo.2021.801689.
348. Pratt-Ubunama MN, Nishizaka MK, Boedefeld RL, Cofield SS, Harding SM, Calhoun DA. Plasma aldosterone is related to severity of obstructive sleep apnea in subjects with resistant hypertension. Chest 2007;131:453–459. doi: 10.1378/chest.06-1442.
349. Gonzaga CC, Gaddam KK, Ahmed MI, Pimenta E, Thomas SJ, Harding SM, *et al*. Severity of obstructive sleep apnea is related to aldosterone status in subjects with resistant hypertension. J Clin Sleep Med 2010;6:363–368. doi: 10.5664/jcsm.27878.
350. Krasinska B, Cofta S, Szczepaniak-Chichel L, Rzymski P, Trafas T, Paluszkiewicz L, *et al*. The effects of eplerenone on the circadian blood pressure pattern and left ventricular hypertrophy in patients with obstructive sleep apnea and resistant hypertension – A randomized, controlled trial. J Clin Med 2019;8:1671. doi: 10.3390/jcm8101671.
351. Yang L, Zhang H, Cai M, Zou Y, Jiang X, Song L, *et al*. Effect of spironolactone on patients with resistant hypertension and obstructive sleep apnea. Clin Exp Hypertens 2016;38:464–468. doi: 10.3109/10641963.2015.1131290.
352. Raina R, Krishnappa V, Das A, Amin H, Radhakrishnan Y, Nair NR, *et al*. Overview of monogenic or mendelian forms of hypertension. Front Pediatr 2019;7:263. doi: 10.3389/fped.2019.00263.
353. Monticone S, Losano I, Tetti M, Buffolo F, Veglio F, Mulatero P. Diagnostic approach to low-renin hypertension. Clin Endocrinol (Oxf) 2018;89:385–396. doi: 10.1111/cen.13741.
354. Liu K, Qin F, Sun X, Zhang Y, Wang J, Wu Y, *et al*. Analysis of the genes involved in Mendelian forms of low-renin hypertension in Chinese early-onset hypertensive patients. J Hypertens 2018;36:502–509. doi: 10.1097/HJH.0000000000001556.
355. Bao M, Li P, Li Q, Chen H, Zhong Y, Li S, *et al*. Genetic screening for monogenic hypertension in hypertensive individuals in a clinical setting. J Med Genet 2020;57:571–580. doi: 10.1136/jmedgenet-2019-106145.
356. Cui Y, Tong A, Jiang J, Wang F, Li C. Liddle syndrome: Clinical and genetic profiles. J Clin Hypertens (Greenwich) 2017;19:524–529. doi: 10.1111/jch.12949.
357. Lim LF, Solmi M, Cortese S. Association between anxiety and hypertension in adults: A systematic review and meta-analysis. Neurosci Biobehav Rev 2021;131:96–119. doi: 10.1016/j.neubiorev.2021.08.031.
358. Carney RM, Freedland KE. Depression and coronary heart disease. Nat Rev Cardiol 2017;14:145–155. doi: 10.1038/nrcardio.2016.181.
359. O'Connor EA, Perdue LA, Coppola EL, Henninger ML, Thomas RG, Gaynes BN. Depression and suicide risk screening: Updated evidence report and systematic review for the US preventive services task force. JAMA 2023;329:2068–2085. doi: 10.1001/jama.2023.7787.
360. O'Connor EA, Henninger ML, Perdue LA, Coppola EL, Thomas RG, Gaynes BN. Anxiety screening: Evidence report and systematic review for the us preventive services task force. JAMA 2023;329:2171–2184. doi: 10.1001/jama.2023.6369.
361. Yamanaka G, Otsuka K, Hotta N, Murakami S, Kubo Y, Matsuoka O, *et al*. Depressive mood is independently related to stroke and cardiovascular events in a community. Biomed Pharmaco-

ther 2005;59(Suppl 1):S31–S39. doi: 10.1016/s0753-3322(05)80007-1.
362. Trudel-Fitzgerald C, Gilsanz P, Mittleman MA, Kubzansky LD. Dysregulated blood pressure: Can regulating emotions help? Curr Hypertens Rep 2015;17:92. doi: 10.1007/s11906-015-0605-6.
363. Zeng GQ, Liu ZT, Gao J, *et al*. The impact of comprehensive interventions on blood pressure in hypertensive patients with comorbid anxiety and depression (in Chinese). Chin J Hyperten 2015;23:880–882.
364. Duan S, Xiao J, Zhao SP, *et al*. The impact of antianxiety treatment on blood pressure and quality of life in hypertensive patients with anxiety symptoms (in Chinese). Chin J Clinical Psychology 2008;16:205–207.
365. Lin HY, Hu SJ. The effects of fluoxetine and empathy techniques on quality of life and anxiety-depressive symptoms in elderly hypertensive patients with depression (in Chinese). Chin J Gerontology 2015;35:1455–1456.
366. Qian H, Tao F, Zhou HL. The effect of amlodipine and citric acid tamsulosin combination therapy on blood pressure circadian rhythm in patients with primary hypertension and anxiety (in Chinese). Chin J Hyperten 2021;29:180–183.
367. Xing HY, Xu XJ, Wang W. The effects of paroxetine on blood pressure and heart rate variability in hypertensive patients with anxiety and depression (in Chinese). Chin J Mod Appl Pharm 2009;26(S1):1188–1191. doo:CNKI:SUN:XDYD.0.2009-S1-039.
368. Yuan M, Xu W, Xu J, *et al*. Stepwise clinical pharmacological intervention in elderly patients with non-white coat hypertension and comorbid anxiety (in Chinese). Chin J Gerontol 2019;39:3345–3348.
369. Fu W, Ma L, Zhao X, Li Y, Zhu H, Yang W, *et al*. Antidepressant medication can improve hypertension in elderly patients with depression. J Clin Neurosci 2015;22:1911–1915. doi: 10.1016/j.jocn.2015.03.067.
370. Bacic-Vrca V, Marusic S, Erdeljic V, Falamic S, Gojo-Tomic N, Rahelic D. The incidence of potential drug-drug interactions in elderly patients with arterial hypertension. Pharm World Sci 2010;32:815–821. doi: 10.1007/s11096-010-9442-5.

How to cite this article: Chinese Society of Cardiology, Chinese Medical Association; Hypertension Committee of Cross-Straits Medicine Exchange Association; Cardiovascular Disease Prevention and Rehabilitation Committee, Chinese Association of Rehabilitation Medicine. Clinical practice guidelines for the management of hypertension in China. Chin Med J 2024;XXX:1–46. doi: 10.1097/CM9.0000000000003431