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CONSENSUS

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Expert consensus on the management of hypertension in the young and middle-aged Chinese population

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Summary

Background and purpose: The increased prevalence of hypertension, along with obesity, dyslipidemia, and type 2 diabetes in the young and middle-aged population has become a major global public health issue. Although more attention has been paid to the management of hypertension and cardiovascular disease (CVD) risks in elderly patients nationally and internationally, there is currently no consensus worldwide on appropriate evaluation and treatment of hypertension in younger subjects. We developed the consensus and aimed to provide a comprehensive strategy for the management of hypertension in young and middle-aged population.

Methods: The authors and experts of the Hypertension Group of the 10th committee of Chinese Society of Cardiology reviewed the available literature and evidence on the pathophysiological characteristics of hypertension, CVD risk assessments and antihypertensive therapies, discussed and reached an agreement on recommendations.

Disccussions and recommendations: The pathophysiological and clinical characteristics of hypertension in young and middle-aged patients are vastly different from those observed in the elderly. In particular, the sympathetic nervous system (SNS) and the renin-angiotensin system (RAS) are significantly activated in this population. Global CVD risk assessment should be performed as determinants of initiating anti-hypertensive therapy. A blood pressure (BP) target of <140/90 mm Hg should be achieved first on BP-lowering therapies, with an ultimate BP <130/80 mm Hg for most patients, if tolerated. Initiating BP-lowering therapies with a beta-blocker or RAS inhibitor (angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker), or in combination with calcium channel blocker or diuretic in high CVD risk patients, along with active lifestyle changes, are preferred.

Conclusions: An aggressive and comprehensive BP and CVD risk management strategy should be implemented in the young and middle-aged hypertensive population.

1 | INTRODUCTION

Hypertension, defined as blood pressure (BP) ≥140/90 mm Hg, is one of the most common, yet reversible, risk factors for cardiovascular disease (CVD). Globally, 9.40 million people died from hypertension in 2010, accounting for 17.8% of total deaths; disability-adjusted life years (DALYs) caused by hypertension were 170 million person-years, or 7.0% of the total global DALYs.[1] Data from China showed that hypertension accounted for 24.6% of all deaths, and 12.0% of total DALYs,[2] and the direct medical cost of hypertension in China has reached 36.6 billion yuan per year.[3]

Hypertension in the young and middle-aged (<65 years old) population is mostly latent and detected by chance. Historically and

currently, more attention has been paid to the management of hypertension and CVD risks in elderly patients. National and international guidelines and expert consensuses have been developed for elderly people,[4-9] despite the facts that the long-term (>10 years) and lifetime risks are higher in young and middle-aged hypertensive subjects, owing to longer life expectancy. Strengthening BP control and systematic management in younger patients will help to reduce the burden of atherosclerotic CVD (ASCVD).

To address these issues, on behalf of the Hypertension Group of the 10th committee of the Chinese Society of Cardiology developed a consensus to provide guidance and advice for the management of hypertension in young and middle-aged adults.

What's known

- The pathophysiology of hypertension in young and middle-aged adults differs from that in elderly subjects, and tends to be associated with metabolic disorders.
- Hypertension in young and middle-aged adults is usually mild and has no typical symptom in comparison with hypertension in elderly subjects.
- CVD risk is increased in young and middle-aged prehypertensive and hypertensive adults, but hypertension awareness, treatment and control rates are low.

What's new

- For young and middle-aged adults, this consensus recommends: accurate diagnosis of hypertension using BP measurements (including the use of ABPM and HBPM); a long-term CVD risk assessment prior to initiating treatment; and a BP target of <140/90 mm Hg (<130/80 mm Hg if tolerable, or in patients with relevant comorbidities).
- Lifestyle interventions are key and should be started early.
- Pharmacologic antihypertensive strategies should be tailored to the individual, and take into account the management of CVD risk factors such as smoking, overweight/obesity, dyslipidemia, diabetes and metabolic syndrome.
- Patients should be monitored and encouraged to share data with doctors for medication adjustment and to improve compliance.

2 | METHODS

Panel members reviewed the available evidence and developed the recommendations. The content was fully discussed during three plenary sessions, and the agreement of more than two-thirds of panel members was required to pass any decision.

3 | EPIDEMIOLOGY

Cardiovascular disease risk increases with the prevalence of prehypertension (systolic/diastolic BP [SBP/DBP] 120-139/80-89 mm Hg) and hypertension in some parts of the world, including China, especially in young and middle-aged individuals.[10-13] In a Chinese cohort study, 65.0% of participants aged 35-59 years with BP 130-139/80-89 mm Hg experienced an increase (≥140/90 mm Hg) and a 3.01-fold increased CVD risk compared with those whose BP was maintained at <130/80 mm Hg during a 15-year follow-up period.[12] Similar CVD mortality data were observed in the younger population from the Chicago Heart Association Detection Project in Industry study during a 31-year follow-up.[13]

Improvements in hypertension awareness, treatment and control rates in the younger and middle-aged population are also needed. According to data from the Chinese Health and Nutrition Survey collected between 2009 and 2010, hypertension awareness rates in males (females) aged ≥60, 45-59, and 18-44 years were 52.1% (62.0%), 37.9% (51.3%), and 20.8% (38.0%), respectively, of whom 44.2% (54.5%), 29.8% (43.2%), and 12.0% (27.3%) were treated and 11.7% (14.8%), 8.0% (9.9%), and 4.3% (9.1%) were controlled, respectively.[14]

4 | PATHOPHYSIOLOGICAL CHARACTERISTICS OF HYPERTENSION

In contrast to the characteristics of arteriosclerosis, volume overload and large arterial stiffening in elderly people with hypertension,[15] peripheral resistance is increased in young and middle-aged hypertensive patients, although in most patients there is no obvious abnormality to arterial elasticity.[16]

Activation of the sympathetic nervous system (SNS) is an important mechanism in young and middle-aged hypertensive patients. BP elevations in the early stages of hypertension are often accompanied by increased heart rate, a biomarker of SNS activation.[17] In one analysis, 64% of patients with hypertension aged <40 years showed evidence of SNS overactivation, compared with 23% of patients aged ≥40 years.[18]

Renin-angiotensin system (RAS) activation is crucial in the occurrence and development of hypertension, particularly in subjects with obesity and metabolic syndrome.[19] In a study of 158 Chinese patients with hypertension, it was found that plasma renin activity and angiotensin II decreased with age,[20] indicating that RAS activation may be an important mechanism for the pathogenesis of hypertension in young and middle-aged patients.

Based on these data, SNS inhibition with beta-blockers, and RAS inhibition with angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs) may contribute to the control of hypertension in young and middle-aged hypertensive patients.

5 | CLINICAL CHARACTERISTICS OF HYPERTENSION

5.1 | Absence of typical symptoms

Most hypertensive patients show no clear symptoms, except for dizziness, headache and other minor symptoms, which only occur in some patients.

5.2 | Most patients classified as mild hypertension

Data from the US National Health and Nutrition Examination Surveys between 2011 and 2012 showed that mild (grade 1) hypertension accounted for 52% of the hypertensive population aged 18-39 years, 32% of those aged 40-59 years and 36% of those aged ≥60 years.[21] A similar trend could be seen in nationwide Chinese Hypertension Survey 2012-2015, as mild hypertension accounted for 74.3% of the hypertensive population aged 18-44 years, 56.7% of those at 45-64 years and 49.0% of those aged >65 years.[11]

5.3 | Elevated DBP is common

Hypertension in young and middle-aged patients is more likely to be isolated diastolic hypertension (IDH), conversely, elderly patients present primarily with isolated systolic hypertension (ISH).[16,22,23] The relatively normal arterial elasticity in a younger population can absorb the additional pressure caused by increased cardiac stroke, resulting in an increased overall peripheral resistance and an elevation in DBP. This lack of large arterial stiffening may also contribute to the absence of notable increases in SBP.[24]

A 22-year follow-up analysis of the Multiple Risk Factor Intervention Trial showed that, even if SBP was normal (<120 mm Hg), the risk of CVD mortality was significantly increased with elevated DBP.[25]

5.4 | High proportion of overweight/obesity and metabolic abnormalities

Coexisting overweight/obesity, dyslipidaemia, impaired glucose tolerance or diabetes and hyperuricemia are relatively high among younger hypertensive patients. A Spanish survey of 6815 people showed that 80.4% of hypertensive patients <55 years had dyslipidaemia, 45.9% had abdominal obesity, >70% had more than two risk factors, and nearly 50% had metabolic syndrome, resulting in an aggregation of CVD risks.[26]

5.5 | Low proportion of home BP measurements

The proportion of young and middle-aged hypertensive patients who perform home BP monitoring (HBPM) is low. A survey of Beijing communities showed that 38.8% of hypertensive patients aged <60 years performed weekly self-BP measurements compared with 46.1% of patients aged ≥60 years.[27] Insufficient monitoring of hypertension in this population is one of the factors affecting BP control.

5.6 | Poor treatment compliance and low BP control rate

Younger patients with hypertension are less likely to adhere to prescribed drug therapy than older patients,[28,29] likely because of heavy workloads, stress and concerns about drug-related toxicity. Together, this results in poorer compliance and lower BP control rates than in older patients. Data from the Beijing community survey showed that ageing was a predictor for increased hypertension control rate.[27]

6 | CLINICAL EVALUATION AND DIAGNOSIS OF HYPERTENSION

Most young and middle-aged hypertensive patients are classified as essential hypertension; the prevalence of secondary hypertension is reported to be 5%-15%.[30] Common causes of secondary hypertension (renal disease, renal artery stenosis, primary aldosteronism [PA], and obstructive sleep apnoea syndrome) must be excluded prior to diagnosis of essential hypertension, especially in younger patients (<40 years) with grade 2 or more severe hypertension. Screening all hypertensive patients for secondary hypertension is not feasible or cost-effective in primary care. We recommend a selective rather than all patients screening strategy, such as in subjects suspecting PA with severe hypertension, spontaneous or diuretic-induced hypokalemia, Aldosterone: Renin activity Ratio (ARR) blood testing before initiating antihypertensive agent is reasonable, if available, as ACEI/ARBs, beta-blockers or diuretics may interfere with ARR, making the results difficult to explain. With positive findings suspecting of secondary hypertension, referring patients to a hypertension specialist or medical centre for further evaluation or treatment is recommended. In addition, hypertension induced by liquorice, corticosteroids, non-steroidal anti-inflammatory drugs, or contraceptive drugs, requires additional attention, particularly in females.[31] Finally, accurate BP measurement and CVD risk assessment before initiating treatment are equally important in young, middle-aged and elderly patients.

6.1 | BP measurement

Accurate BP measurement is the basis for the diagnosis of hypertension. In addition to traditional office BP (OBP) measurement, out-of-office measurements, including ambulatory BP monitoring (ABPM) or HBPM, have been actively recommended by recent hypertension guidelines.[4,5,7] The UK National Institute for Clinical Excellence (NICE) hypertension guideline recommends using ABPM to confirm a hypertension diagnosis if BP is >140/90 mm Hg during the first clinic visit.[32] The Canadian Hypertension Education

Program advises a diagnosis of hypertension if the mean 24-hour BP is ≥130/80 mm Hg,[33] while the Japanese hypertension guidelines suggest a HBPM measurement ≥135/85 mm Hg or mean 24-hour BP ≥130/80 mm Hg as indicators of hypertension.[34]

In China, ABPM is not widely performed, except in secondary and tertiary city hospitals. HBPM in urban areas has increased in recent years, but the utilisation rate and overall knowledge level remain low.[27,35] OBP measurement currently remains the gold standard for the diagnosis of hypertension in China. However, OBP measurement alone is not enough to accurately diagnose 'white coat hypertension' or exclude 'masked hypertension', which are common in young and middle-aged hypertensive patients. Therefore, for newly diagnosed patients with high OBP values, ABPM or HBPM is recommended to confirm the diagnosis, if available. Active use of HBPM and understanding the dynamics of BP through self-measurement can help to eliminate treatment inertia, and thus improve BP control.[36]

6.2 | Global CVD risk assessment

Compared with the elderly population, most young and middle-aged patients with hypertension are characterised with shorter hypertension duration, less hypertension-mediated organ damage (HMOD) and complications in the early stages, and more low-to-moderate CVD risks.[5]

While global CVD risks in this population are not high in the short term (5-10 years), the long-term (>10 years) and lifetime CVD risks are high. A survey in 61 585 US adults aged >55 years without CVD showed that lifetime CVD risk was 42%-69% in patients with hypertension, compared with only 22%-41% for those whose BP was maintained or decreased to within a normal range.[37]

A large cohort study of young males (mean age 18.4 years) in Sweden found a strong correlation between BP (particularly DBP) and CVD and all-cause mortality after a mean follow-up of 24 years.[38] Nearly 20% of deaths could be attributed to increased DBP.[38]

A recently developed ASCVD risk assessment model based on the China-PAR project was validated against the 10-year and long-term CVD risks observed in China,[39] and could be applied to hypertension and CVD risk management in the young and middle-aged population.

6.3 | Other measurements

Urine analysis, blood glucose, lipid profiles, electrolytes, liver and kidney function tests and electrocardiograms should be examined routinely. In addition, evaluation of HMOD, such as left ventricular hypertrophy and microalbuminuria should be considered, according to the guidelines.[4,5]

7 | ANTIHYPERTENSIVE THERAPY

Antihypertensive drug therapy should be administered alongside lifestyle interventions, particularly in patients with grade 2 or 3 hypertension, those with established CVD, or those at high CVD risk. For uncomplicated grade 1 hypertension, there is controversy about whether antihypertensive drug therapy should be initiated as prior clinical trials seldom included younger hypertensive patients at low-to-moderate CVD risk. However, epidemiological studies have demonstrated a clear relationship between BP and the long-term risk of CVD events in young adults with a BP >130/80 mm Hg.[38,40] Furthermore, earlier treatment can prevent the development of severe hypertension and HMOD, which, if left untreated, may not be completely reversible.[41] Thus, despite the absence of data from randomised controlled trials that demonstrate the benefits of antihypertensive treatment in younger adults with uncomplicated grade 1 hypertension, treatment with BP-lowering drugs may still be considered prudently.[5] In this situation, patient-clinician discussions are recommended to guide the decision-making process.

The following principles of treating hypertension should be considered: (a) early intervention, (b) lifestyle changes, (c) drug therapy, (d) treating to BP target to minimise CVD morbidity and mortality and (e) comprehensive management of other reversible CVD risk factors, such as obesity, dyslipidaemia and hyperglycaemia. Based on the pathophysiological and clinical characteristics of hypertension in this population, the intensity of lifestyle intervention and optimal drug therapy for young and middle-aged hypertension patients might be different from that of elderly patients.

Figure 1 summarises recommendations for the treatment of hypertension in young and middle-aged patients.

7.1 | BP targets

The optimal BP treatment target is still controversial, even after the publication of the Systolic Pressure Intervention Trial.[42,43] American guidelines changed the definition of hypertension and BP target from <140/90 to <130/80 mm Hg.[7] The 2018 European hypertension guidelines recommended a BP target of <140/90 mm Hg for all patients and <130/80 mm Hg for most, if treatment was tolerated.[5]

Therefore, currently, for young and middle-aged hypertensive patients without complications, it is generally recommended that BP treatment targets should be <140/90 mm Hg, and if tolerated, <130/80 mm Hg.[4] For patients with diabetes or heart failure, BP should be lowered to <130/80 mm Hg, or according to the relevant guidelines.

7.2 | Non-drug therapy

Non-drug therapy mainly refers to lifestyle interventions, which involve cessation of behaviours and habits that are harmful to physical and mental health. These therapeutic lifestyle changes should be initiated early and may also help to improve BP-lowering treatment efficacy and reduce CVD risk. Lifestyle changes include: (a) restricting salt intake (<6 g daily), increasing potassium-rich food (fresh fruits, vegetables and beans) and reducing saturated fat and cholesterol intake; (b) weight control (body mass index [BMI] <24 kg/m^2; waist

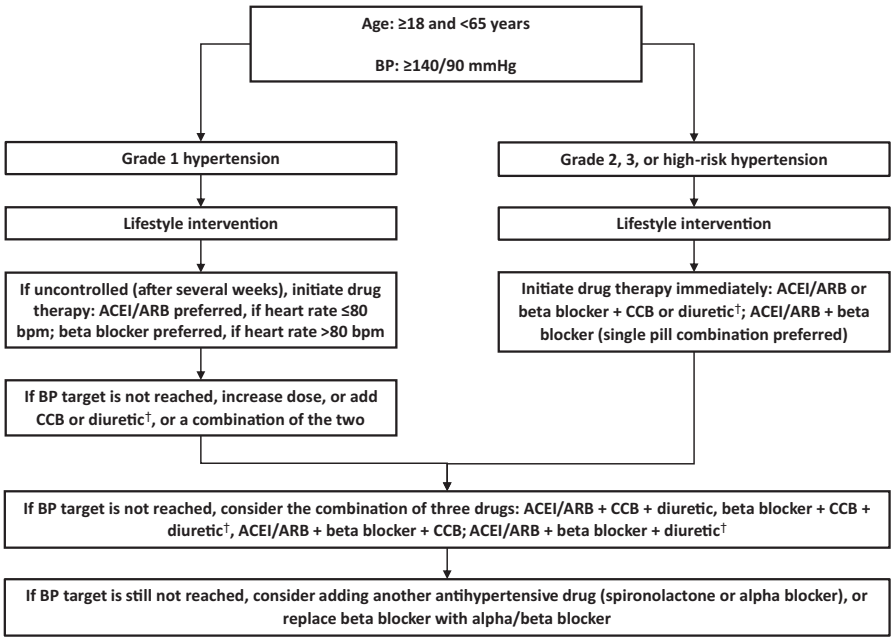

FIGURE 1 Treatment algorithm for young and middle-aged patients with hypertension. †The combination of beta-blockers and diuretics should be used with caution in patients concomitant with metabolic syndrome or diabetes. Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; CCB, calcium channel blocker

circumference: men <90 cm, women <85 cm); (c) smoking cessation (quitting smoking and avoiding second-hand smoke); (d) limiting daily alcohol intake (men <25 g, women <15 g); (e) aerobic exercise (such as walking, jogging, cycling or swimming, etc; daily physical activity for >30 minutes, 5-7 times/week); and (f) reducing mental/psychological stress (seeking professional psychological counselling when necessary).

Non-drug therapy is particularly important for young and middle-aged hypertensive patients, as early intervention is critical for slowing the progression of hypertension and subsequent CVD. Furthermore, younger patients can better tolerate higher intensity physical exercise than elderly people, which might be beneficial for body weight control, cardiopulmonary function improvement, and even for mental and psychological health. Healthy lifestyle changes, such as reducing salt and fat intake, smoking cessation and increasing exercise, have a better cost-effectiveness ratio than drug therapy, and are important strategies for the prevention and treatment of hypertension and CVD.[44,45]

7.3 | Drug therapy

For young and middle-aged patients with mild hypertension (<160/100 mm Hg, grade 1 hypertension), drug therapy should only be initiated if several weeks of lifestyle intervention have not reduced BP sufficiently. For patients whose BP exceeds 160/100 mm Hg (grade 2 or 3), or who are at high CVD risk, drug therapy should be initiated immediately. Long-acting, once-daily preparations are preferred.

There are five classes of antihypertensive drugs (diuretics, beta-blockers, calcium channel blockers [CCBs], ACEIs and ARBs) which could be used as an initial treatment option for young and middle-aged patients with hypertension. Randomised controlled trials have shown efficacy differences in younger populations, with ACEIs and beta-blockers being superior to thiazide diuretics and CCBs,[46-48] although data are limited. In clinical practice, DBP control is suboptimal with diuretics and CCBs, especially in IDH. Therefore, to achieve effective BP control, it is necessary to initiate appropriate antihypertensive drugs or strategies based on the pathophysiological mechanisms of hypertension in the young and middle-aged population.

Laragh proposed classifying hypertensive patients into 'high renin type' (R type, which is mostly found in the younger population) and 'low renin type' (also called high volume type or V type, which is mostly found in elderly people), based on plasma renin activity.[49] The British Hypertension Society had previously proposed the 'AB/CD' rule for the selection of initial antihypertensive drugs based on the pathophysiology of hypertension at different ages. Initial treatment with antihypertensive drugs should involve either renin inhibitors (ACEIs/ARBs or beta-blockers) or volume inhibitors (CCBs or diuretics) for hypertensive patients <55 and ≥55 years old, respectively.[50,51] This recommendation has been retained in subsequent guideline updates in the UK and other countries.[32,52]

Sympathetic nervous system inhibition with beta-blockers is as effective as other treatments in reducing BP and preventing cardiovascular events in young and middle-aged hypertensive patients.[53,54] Beta-blockers were originally thought to be less effective in preventing stroke than CCBs and ARBs,[55,56] but this was not confirmed in patients <65 years in a recent meta-analysis.[54]

The UK NICE and US hypertension guidelines removed beta-blockers off the first-line BP-lowering agents,[7,32] as in LIFE trial and ASCOT, an atenolol-based strategy, alone or combined with thiazide is inferior to losartan or amlodipine-based therapy in stroke and CVD prevention in hypertensive patients with left ventricular hypertrophy or at high risk.[57,58] Beta-blockers are a class of BP-lowering agent with heterogeneity, and the results of atenolol should not be speculated to other non-atenolol beta-blockers, especially those

with higher beta1-selectivity, vasodilation or anti-oxidative properties, such as bisoprolol, metoprolol, carvedilol or nebivolol. The new released Chinese and European hypertension guidelines insist on recommending beta-blockers, along with the other four class of antihypertensive agents as an initial option.[4,5] This is critically important for the younger population with hypertension, especially for those with overt sympathetic activation, as indicated clinically with an increased heart rate (>80 beats/min). With the socio-economic transition in China, younger people have to face more stress than before, which inevitably increasing SNS activation, especially in younger hypertensive subjects. In a large survey included more than 110 thousand hypertensive patients in China, 38.2% hypertensive patients without complications have a resting heart rate ≥80 beats/min. Generally, heart rate is faster in younger subjects or beta-blockers naive patients.[59]

Beta-blockers should be used with caution when combined with diuretics in patients with diabetes or metabolic syndrome, owing to potential effects on glucose and lipid metabolism.[52] However, beta-blockers could be used in younger hypertensive patients, especially in those with significant SNS activation (eg, resting heart rate >80 beats/min), or in special conditions, such as complicated with coronary artery disease or chronic heart failure.

RAS inhibitors have demonstrated BP-lowering effects and target organ protection; a meta-analysis of 20 hypertension clinical trials showed that ACEIs reduced all-cause mortality versus placebo or other antihypertensive drugs.[60] Moreover, another meta-analysis found no differences in major CVD when controlling for BP differences between RAS inhibitors and other antihypertensive agents.[55]

The NICE hypertension guidelines[32] recommend that drug therapy for hypertensive patients <55 years start with an ACEI (or an ARB, if ACEI is not tolerated), while US community guidelines recommend ACEIs or ARBs as first-line therapy for grade 1 hypertension without complications, but only in non-Black patients aged <60 years.[52] RAS activation was found to be more significant in patients with obesity, dyslipidaemia, smoking or other CVD risk factors,[61-63] thus, RAS inhibitors are particularly suitable for these patients.[19,64]

Of note, as of the risk of teratogenicity with RAS inhibitors, ACEIs or ARBs should not be used in younger hypertensive women planning pregnancy or of childbearing potential. In that case, beta-blockers, especially labetalol will be preferred as an alternative.

Blood pressure control is not optimal in young and middle-aged patients with hypertension. Studies in France[65] and China[66] found that less than one-third of patients aged <59 years had controlled BP, providing a compelling argument for initiating rational combination therapy as early as possible, especially in high-risk patients with poor BP control. Drug combinations should be based on RAS inhibitors or beta-blockers, combined with dihydropyridine CCBs or a thiazide/thiazide-like diuretic (with the caveat of potential metabolic risk when combining a diuretic with a beta-blocker). For patients with elevated DBP (including IDH) and resting heart rate (>80 beats/min), a RAS inhibitor and beta-blocker combination should be considered. Single pill combinations help to increase therapeutic compliance, and should be considered as a priority. The combination of an ACEI with an ARB is not recommended.[67]

In hypertensive patients with diabetes, chronic kidney disease, coronary heart disease or heart failure, appropriate antihypertensive drugs should be selected according to the relevant guidelines.

8 | FOLLOW-UP AND DUAL REFERRAL

Patients should be monitored, with medication regimens adjusted as necessary. The interval of follow-up should be based on the patient's CVD risk and BP level. In general, patients with grade 1 hypertension or low-to-moderate CVD risk should be followed up every 1-3 months, and patients with grade 2 or 3 hypertension or those with high CVD risk should be followed up every 2-4 weeks. The interval of follow-up can then be appropriately prolonged after stable BP control is achieved. It is important to evaluate the control of other CVD risk factors and HMOD during follow-up, with reference to hypertension guidelines.[4,5]

With established diagnosis of hypertension and stable clinical condition and BP control, patients could be referred to primary care or community health service for further follow-up. For those with severe BP fluctuation, resistant to treatment, suspected with secondary hypertension or worsened clinical condition, referring to hypertension specialist or transferring to medical centre are necessary.

With the development of intelligent BP measurement devices, BP data can be recorded and shared simultaneously. Sharing data with physicians may be of help in making timely medication adjustments, and improving BP control.

9 | MANAGEMENT OF ASSOCIATED CVD RISK FACTORS

The comprehensive evaluation and management of CVD risk factors in young and middle-aged hypertensive patients should be an important primary prevention strategy, and should include smoking cessation, body weight control, statin use for hypercholesterolaemia (Table 1), and diabetes or metabolic syndrome control.[68,69]

The benefits of low-dose aspirin in the secondary prevention of CVD clearly outweigh the risks of bleeding, and aspirin is uniformly recommended in this setting. However, controversies have been existed about whether, and if so in whom, aspirin is appropriate for the primary prevention of CVD till the recent three trials of low-dose aspirin versus placebo in populations at increased risk but without established CVD were reported. In the ARRIVE trial for people at low risk of CVD, aspirin had no effect on major CV events but increased gastrointestinal bleeding.[70] In the ASCEND trial for patients with diabetes mellitus and no evidence of vascular disease, the benefits of aspirin on serious vascular events reduction were totally offset by the increased risk of

TABLE 1 Hypertension and LDL-C levels and treatment targets[69]

Hypertension and risk factors	LDL-C level (mmol/L)	ASCVD risk	LDL-C target (mmol/L)
Hypertension	1.8 to <4.9	Low	<3.4
Hypertension + 1 risk factor	1.8 to <2.6	Low	<3.4
Hypertension + 1 risk factor	2.6 to <4.9	Moderate	<3.4
Hypertension + 2 risk factors	1.8 to <2.6	Moderate	<3.4
Hypertension + 2 risk factors	2.6 to <4.9	High	<2.6
Hypertension + 3 risk factors	1.8 to <4.9	High	<2.6
Hypertension	≥4.9	High	<2.6
Hypertension + diabetes (≥40 y old)	1.8 to <4.9	High	<2.6
Hypertension + ASCVD	—	Very high	<1.8

Note: Other risk factors include age (male ≥45 y, female ≥55 y), smoking, low high-density lipoprotein cholesterol (HDL-C <1.0 mmol/L).
Abbreviations: ASCVD, arteriosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol.

major bleeding.[71] The ASPREE trial in elderly people was terminated early since aspirin had no effect on disability-free survival but significantly increased the risk of major haemorrhage and, unexpectedly, all-cause mortality.[72] Based on recent evidence, US primary prevention guidelines have provided a prudent recommendation regarding aspirin for primary prevention.[73] Generally, aspirin (75-100 mg daily) is only indicated at those hypertensive patients with established CVD for secondary prevention, or those at 40-70 years with higher CVD risk but not at increased risk of bleeding in the primary prevention setting.

10 | SUMMARY OF RECOMMENDATIONS

The management of hypertension in the young and middle-aged population includes the following recommendations:

- Encourage the use of HBPM to confirm the diagnosis of hypertension.
- Screen for CVD risk factors and conduct a global CVD risk assessment.
- Target BP to <140/90 mm Hg for all, and to <130/80 mm Hg for most patients, if tolerated. For patients with comorbidities such as diabetes or heart failure, individualised BP management should be applied, following the relevant guidelines.
- Advocate active lifestyle intervention as an effective means of hypertension management.
- For patients without complications, any of the five classes of antihypertensive agents can be used as an initial treatment option. As SNS or RAS activation is more common in the young and middle-aged population, beta-blockers and RAS inhibitors (ACEIs or ARBs) are effective in lowering BP (especially DBP) in these patients and are preferred. Beta-blockers are especially suitable for patients with elevated heart rate, coronary heart disease or heart failure, while ACEIs or ARBs are preferred for patients with metabolism disorders, or chronic kidney disease (stage 3a or above to reduce albuminuria and the risk of end-stage renal disease). ACEIs or ARBs are also recommended for patients with coronary heart disease or heart failure (with the same priority as beta-blockers).
- Initiate combination therapy in high-risk patients, including those with multiple CVD risk factors, grade 2 or 3 hypertension, or in cases of lack of efficacy with monotherapy. An ACEI or ARB combined with a dihydropyridine CCB or thiazide/thiazide-like diuretic is recommended as a priority; but a beta-blocker combined with a CCB or diuretic can also be used (the latter should be used with caution for those with metabolism disorders), or an ACEI or ARB combined with a beta-blocker in patients with elevated DBP and heart rate. The combination of an ACEI with an ARB is not recommended.
- Initiate an active, integrated prevention and treatment strategy for patients with hypertension and comorbid risk factors.

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DISCLOSURE

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

The corresponding authors proposed and initiated the writing of this consensus. The first author wrote the outline and the first draft of the manuscript, and all authors participated in manuscript revisions.

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