MINISTRY OF HEALTH
SINGAPORE

Hypertension

MOH Clinical Practice Guidelines 1/2017

Chapter of Family Medicine Physicians
Academy of Medicine, Singapore

Chapter of Endocrinologists
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Singapore Hypertension Society

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November 2017

Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
1^{++}	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1^{+}	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2^{++}	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1^{++} and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1^{++} or 1^{+}
C	A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2^{++}
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2^{+}
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL PRACTICE GUIDELINES

Hypertension

MOH Clinical Practice Guidelines 1/2017

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Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Such standards are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines might not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care.

Contents

Foreword

In the Global Burden of Disease 2010 study, hypertension is the leading associated risk factor for cardiovascular disease. High blood pressure accounts for 9.4 million deaths and 7.0% of global disability-adjusted life years (DALYs) worldwide.* These adverse outcomes exceed those due to elevated BMI, fasting plasma glucose, and total cholesterol combined.

Hypertension is prevalent and increasing in many developing and developed countries. In Singapore, the 2010 National Health Survey showed a decreasing trend in the crude prevalence of hypertension among Singapore residents aged between 30 and 69 years, from 27.3% in 1998 to 24.9% in 2004, and down to 23.5% in 2010.† However, the age-specific prevalence for hypertension rises markedly from age 40 years onwards and, with our ageing population, we continue to face challenges in the prevention and control of hypertension.

The last hypertension guidelines were published in 2005. Many important studies have since been published, and it is timely to update the hypertension guidelines to include new findings and evidence-based recommendations. The new guidelines continue to adhere to the fundamental principles of diagnosing, evaluating and treating high blood pressures.

It is hoped that this set of guidelines will assist doctors in managing patients with hypertension cost-effectively, with maximal benefits and minimal risks, to further reduce the prevalence of hypertension in Singapore.

ASSOCIATE PROFESSOR BENJAMIN ONG
DIRECTOR OF MEDICAL SERVICES

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*Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2013; 380:2224-2260.

†Epidemiology and Disease Control Division Ministry of Health Singapore. National Health Survey 2010 Report.

Commonly used abbreviations

The following is a list of abbreviations commonly used in this set of guidelines (arranged in alphabetical order), and a description of what they represent:

- ABPM ambulatory blood pressure monitoring
- ACE angiotensin-converting enzyme
- ACR albumin:creatinine ratio
- ARB angiotensin II receptor blocker
- BMI body mass index
- BP blood pressure
- CAD coronary artery disease
- ECG electrocardiography
- eGFR estimated glomerular filtration rate
- HBPM home blood pressure monitoring
- LVH left ventricular hypertrophy
- NHS National Health Survey
- PCR protein:creatinine ratio
- RAAS renin-angiotensin-aldosterone system
- RCT randomised controlled trial

List of recommendations

Details of recommendations appear in the main text at the pages indicated. The key recommendations are highlighted in brown.

Classification of hypertension

No.	Recommendation	Grade, Level of Evidence	CPG page no.
1	Classify hypertension according to systolic BP and diastolic BP levels. When the systolic BP and the diastolic BP fall into different categories, the higher category applies.	Grade D, Level 4	18

Measuring blood pressure

No.	Recommendation	Grade, Level of Evidence	CPG page no.
2	Use the following procedures when recording BP: 1. Allow the patient to sit or lie down for at least 3 minutes before measuring the BP. 2. The patient should refrain from smoking or taking caffeinated drinks during the 30 minutes before measurement. 3. Use a cuff with a bladder 12-13 cm x 35 cm in size. A cuff with a larger bladder should be used for large upper arms; where a thigh cuff should be used for extremely large arms. 4. When using the auscultatory method, use the disappearance of phase V Korotkoff sounds to measure the diastolic BP. 5. Measure the BP in both arms at the first visit; subsequently re-measure BP on the arm with the higher reading, if applicable. 6. Take 2 or more readings separated by 2 minutes. Average these two values. If the first two readings differ by 5 mmHg or more, further readings should be obtained and averaged.	Grade D, Level 4	19

No.	Recommendation	Grade, Level of Evidence	CPG page no.
	7. In elderly subjects and diabetic patients, measure the BP in the supine (or sitting) position, and within 2 minutes after standing, to record any postural fall in BP. 8. Place the manometer cuff at the level of the heart, regardless of the position of the patient.		
3	Wherever practicable, HBPM or ABPM (in that order) should be offered to younger patients, and to those whom target organ damage is found without a raised clinic BP.	Grade D, Level 4	20
4	The preferred manometer is an automated oscillometric device, with or without memory.	Grade C, Level 2^+	21
5	To ensure reliable values, the patient or carer needs training in device use, and a BP log-book (for basic devices without memory).	Grade D, Level 4	21
6	ABPM is recommended whenever in doubt about the diagnosis, e.g. to confirm borderline hypertension or abnormal results from HBPM.	GPP	21
7	ABPM is also indicated for older, cognitively impaired, anxious or obsessive patients, in whom HBPM might be unreliable or inappropriate.	GPP	21
8	Patients with an average BP ≥135/85 mmHg measured repeatedly at rest at home may be regarded as hypertensive.	Grade D, Level 3	22
9	Patients with a 24-hour ABPM average BP ≥130/80 mmHg, or a daytime average BP ≥135/85 mmHg, or a night-time average BP ≥120/70 mmHg, are regarded as hypertensive.	Grade D, Level 4	22

Evaluating high blood pressure

No.	Recommendation	Grade, Level of Evidence	CPG page no.
10	Routine clinical evaluation of a patient with elevated BP includes the following: 1. Clinical and family history 2. Full standard physical examination 3. Laboratory investigations, including: a) Urine analysis: Dipstick for hematuria/albumin, microscopic examination, and test for albuminuria b) Measurement of serum concentrations of electrolytes, creatinine, urea, fasting glucose and fasting lipids c) Computation of estimated glomerular filtration rate (eGFR) 4. 12-lead electrocardiography (ECG)	Grade D, Level 4	24

Stratifying risk and approach to hypertension management

No.	Recommendation	Grade, Level of Evidence	CPG page no.
11	Assess the overall cardiovascular risk and the patient's BP to guide the management of high BP.	GPP	26
12	Refer to the locally adapted Framingham Risk Score to estimate cardiovascular risk.	Grade D, Level 4	26
13	Offer to start drug treatment immediately in patients with hypertension and existing high cardiovascular risk.	GPP	26
14	Take the BP and other prognostic factors into account when deciding on the management of hypertensive patients.	Grade D, Level 4	26

No.	Recommendation	Grade, Level of Evidence	CPG page no.
15	For high or very high risk individuals, begin immediate drug treatment for hypertension when other risk factors or conditions are present.	Grade A, Level 1^{++}	28
16	For medium risk individuals, monitor the BP and other risk factors for several weeks, and obtain further information, before deciding whether to begin drug treatment.	Grade B, Level 1^{+}	28
17	For low risk individuals, observe the patient over a significant period of time before deciding whether or not to begin drug treatment.	Grade B, Level 1^{+}	28

Treating high blood pressure

No.	Recommendation	Grade, Level of Evidence	CPG page no.
18	Wherever possible, use a team-based approach to manage a patient with hypertension, involving trained nurses and pharmacists with medical practitioners.	Grade A, Level 1^{+}	30
	Lifestyle modification		
19	Recommend lifestyle changes to all hypertensive patients, and in patients with high normal BP. However, drug treatment should not be delayed without reason beyond 3 to 6 months if indicated.	Grade A, Level 1^{+}	31
20	Advise patient to restrict salt intake to 5 to 6 g per day.	Grade A, Level 1^{+}	31
21	Moderate alcohol consumption to no more than 2 standard drinks per day for men, and to no more than 1 standard drink per day for women.	Grade A, Level 1^{+}	31

No.	Recommendation	Grade, Level of Evidence	CPG page no.
22	Increase the consumption of vegetables, fruits, low-fat dairy products, and decrease the intake of saturated and total fats.	Grade A, Level 1^+	31
23	Unless contraindicated, advise patients to reduce weight to a body mass index (BMI) below 23 kg/m^2 and to a waist circumference below 90cm in men, and below 80cm in women (for Asians).	Grade B, Level 2^+	31
24	Advise patients to do at least 30 minutes of moderate dynamic exercise 5 to 7 days per week. Any physical exercise above the basal level, up to 150 minutes/week, confers incremental cardiovascular and metabolic benefits, including BP reduction.	Grade A, Level 1^+	32
25	Advise and offer assistance to all smokers to quit smoking.	Grade A, Level 1^+	32
	Pharmacological treatment		
26	Begin appropriate combination treatment in patients whose pretreatment BP is raised (i.e. ≥ 140/90 mmHg), and specifically in patients whose BP is severely raised (≥ 180/110 mmHg), as they will require two or more drugs for adequate BP control.	Grade B, Level 2^+	33
27	Initiate treatment at low doses of drugs, either singly or as a two-drug combination, to minimise side effects.	Grade D, Level 4	33
28	If an adequate dose of the first drug used demonstrated limited response or was poorly-tolerated, change to a different drug class instead of increasing the dose of the first drug.	Grade A, Level 1^+	33
29	Add a second drug when a single drug fails to achieve target BP.	Grade B, Level 1^+	34

No.	Recommendation	Grade, Level of Evidence	CPG page no.
30	Use long-acting drugs which provide 24-hour efficacy daily.	Grade B, Level 2^{+}	34
31	In hypertensive patients without compelling indications or contraindications for any particular drug, consider any one, or an appropriate combination, of the five major classes of drugs as the initial treatment.	Grade B, Level 2^{+}	34
32	Take compelling indications and contraindications into account when prescribing an antihypertensive drug (Table 7).	Grade A, Level 1^{+}	34
33	Be aware of the cost of treatment in selecting antihypertensive drugs.	Grade D, Level 4	37
34	Generic formulations which usually cost less than newer non-generic (i.e. proprietary) drugs are acceptable for use.	Grade D, Level 4	37
35	Do not offer aldosterone (mineralocorticoid) antagonists (e.g. spironolactone) to patients with chronic kidney disease (eGFR < 45 ml/min), in particular when combined with an ACE inhibitor or ARB. This is because of the risks of further renal function impairment, and of hyperkalaemia. An aldosterone antagonist might be considered in patients with resistant hypertension after a full work-up has excluded secondary hypertension (Table 4).	Grade C, Level 2^{+}	38
36	Prescribe a diuretic with caution as initial treatment in patients with uncomplicated hypertension, who are at risk for diabetes, because it might cause hyperglycaemia.	Grade B, Level 2^{+}	38
37	Use beta-blockers with caution in patients at risk of developing diabetes, as it raises blood glucose concentrations.	Grade A, Level 1^{+}	38

No.	Recommendation	Grade, Level of Evidence	CPG page no.
38	Use the following drug combinations to treat hypertension: 1. Calcium-channel blocker (dihydropyridine type) plus ACE inhibitor or ARB 2. Calcium-channel blocker plus diuretic 3. Diuretic plus ACE inhibitor or ARB 4. Beta-blocker plus calcium-channel blocker (see caveat in Figure 2) 5. Beta-blocker plus diuretic (see caveat in Figure 2).	Grade B, Level 2^{++}	39
39	Avoid treating patients with an ACE inhibitor plus ARB combination, particularly patients who have chronic kidney disease.	Grade B, Level 1^{+}	39
40	Beware of an increased risk of diabetes mellitus when offering a beta-blocker plus diuretic combination to patients with risk factors such as obesity or metabolic syndrome.	Grade B, Level 2^{++}	39
41	Do not offer renal sympathetic denervation for routine treatment of resistant hypertension.	Grade A, Level 1^{+}	40
42	Do not offer carotid-sinus baroreceptor reflex activation for routine treatment of resistant hypertension.	Grade B, Level 2^{++}	40

Treatment goals and follow up

No.	Recommendation	Grade, Level of Evidence	CPG page no.
43	The recommended target BP treatment levels are: 1. BP < 140/90 mmHg in patients aged under 80 years 2. BP < 150/90 mmHg in patients aged 80 years or older In fragile elderly individuals, the systolic BP goals should be adapted to individual tolerability.	Grade A, Level 1^{+}	41

No.	Recommendation	Grade, Level of Evidence	CPG page no.
44	Patients with the following problems should be referred to a hypertension specialist or clinic: 1. Conditions needing emergency or urgent treatment, e.g. malignant hypertension, hypertensive heart failure, or other impending complications 2. Hypertension that is difficult to manage, e.g. unusually labile BP, or hypertension refractory to multiple drugs in different pharmacological classes 3. Secondary hypertension, i.e. hypertension due to an underlying cause, such as hyperaldosteronism 4. Hypertension in special circumstances, e.g. pregnancy, and young children.	Grade D, Level 4	43

Treating high blood pressure in special conditions

No.	Recommendation	Grade, Level of Evidence	CPG page no.
	Type 2 diabetes mellitus		
45	For patients with type 2 diabetes mellitus who have hypertension, an acceptable treatment target BP is below 140/80 mmHg.	Grade B, Level 2^+	44
46	Use ACE inhibitor, ARB, or calcium-channel blocker as first-line treatment in patients with diabetes without chronic kidney disease or proteinuria.	Grade A, Level 1^+	44
47	Optimised BP control is recommended to reduce the risk, or slow the progression, of diabetic nephropathy.	Grade A, Level 1^+	46

No.	Recommendation	Grade, Level of Evidence	CPG page no.
48	Treat patients with diabetic nephropathy to a target below 140 mmHg systolic BP.	Grade A, Level 1^{+}	46
49	If a diabetic nephropathy patient has severe albuminuria (equivalent to urinary albumin:creatinine ratio (ACR) more than 30 mg/mmol, or urinary PCR more than 50 mg/mmol), consider target below 130 mmHg systolic BP provided GFR changes are monitored carefully.	Grade B, Level 2^{+}	47
50	Treat diabetic chronic kidney disease patients with moderate albuminuria (urinary ACR 3-30 mg/mmol, or PCR between 15-50 mg/mmol) to a target BP equal to or below 130/80 mmHg.	Grade D, Level 4	47
51	Use an ACE inhibitor or ARB as first-line treatment, whenever treatment with BP-lowering drugs is indicated in diabetic nephropathy.	Grade A, Level 1^{+}	48
52	In diabetic nephropathy, if one class of RAAS blocker (either ACE inhibitor or ARB) is not tolerated, replace it with the other class.	Grade D, Level 4	48
53	Combination treatment with both an ACE inhibitor and an ARB should not be routine in diabetic nephropathy.	Grade A, Level 1^{+}	48
54	When ACE inhibitors, ARBs, or diuretics are used in diabetic nephropathy, it is recommended to monitor the serum creatinine and potassium levels for the possible development of acute kidney injury and hyperkalemia.	Grade D, Level 4	48
55	Beta-blockers, calcium-channel blockers, and thiazides are all appropriate second-line therapy in diabetic nephropathy.	Grade A, Level 1^{+}	49

No.	Recommendation	Grade, Level of Evidence	CPG page no.
	Non-diabetic chronic kidney disease		
56	Treat non-diabetic, non-proteinuric chronic kidney disease patients to a target BP below 140/90 mmHg.	Grade A, Level 1^{+}	50
57	Treat non-diabetic chronic kidney disease patient with severe albuminuria to a target BP equal to or below 130/80 mmHg.	Grade A, Level 1^{+}	50
58	Treat non-diabetic chronic kidney disease patients with moderate albuminuria to a target BP equal to or below 130/80 mmHg.	Grade D, Level 4	50
59	Use either an ACE inhibitor or an ARB as the first-line drug, whenever treatment with BP-lowering drugs is indicated in non-diabetic chronic kidney disease patients.	Grade A, Level 1^{+}	50
60	Combination treatment with both an ACE inhibitor and an ARB should not be routinely prescribed in non-diabetic chronic kidney disease patients.	Grade A, Level 1^{+}	50
	Stroke		
61	Where systolic BP is above 140 mmHg but below 220 mmHg within the first two weeks of onset of acute ischaemic stroke, lowering of high BP should be based on individual clinical judgment after careful consideration of all the contraindications.	Grade A, Level 1^{++}	51
62	It is reasonable to lower, with care, a markedly elevated BP (systolic BP above 220 mmHg or diastolic BP above 120 mmHg, or both) by 10% to 15% during the first 24 hours after the onset of acute ischaemic stroke.	Grade D, Level 4	52

No.	Recommendation	Grade, Level of Evidence	CPG page no.
63	After the acute phase of stroke, begin antihypertensive treatment in hypertensive patients if the systolic BP is more than 140 mmHg and diastolic BP is more than 90 mmHg.	Grade D, Level 4	52
64	Use any of the five major pharmacological classes of antihypertensive drugs for stroke prevention in patients during the acute phase of stroke, provided that the BP is effectively lowered.	Grade A, Level 1^{++}	53
65	The target BP level in patients after a transient ischemic attack and after acute phase stroke should be individualised, with careful consideration of medical comorbidities. A lower systolic BP target might benefit a patient who has small vessel disease, but might harm a patient with severe cerebrovascular stenosis.	GPP	53
	Pregnancy		
66	Even though the classification of mild, moderate and severe hypertension by BP level is different in pregnancy, pharmacological treatment is recommended in pregnant women with chronic hypertension who have a persistently elevated systolic BP of 150 mmHg or greater, or a diastolic BP of 100 mmHg or greater.	Grade D, Level 4	54
67	Avoid aggressive rates of lowering of BP in pregnant women with chronic hypertension because of the potential risk of compromising the uteroplacental blood flow.	GPP	54
68	In pregnant women with no target organ damage, and uncomplicated chronic hypertension, aim to keep the BP below 150/100 mmHg.	Grade D, Level 4	54

No.	Recommendation	Grade, Level of Evidence	CPG page no.
69	In pregnant women with target organ damage secondary to chronic hypertension, aim to keep the BP below 140/90 mmHg.	Grade D, Level 4	54
70	In pregnant women with uncomplicated chronic hypertension, do not use drug treatment to decrease the diastolic BP below 80 mmHg.	Grade D, Level 4	54
71	Treat pregnant women with chronic hypertension using methyldopa, labetalol, nifedipine, or a combination thereof.	Grade D, Level 4	54
72	Methyldopa, labetolol, and nifedipine are also considered safe for use during breastfeeding postpartum.	GPP	54
73	ACE inhibitors, ARBs, direct renin inhibitors (e.g. aliskiren), and aldosterone antagonists should be avoided during pregnancy.	Grade D, Level 4	55
	Elderly patients		
74	In elderly hypertensive patients whose systolic BP is 160 mmHg or higher, the BP should be reduced to below 150/90 mmHg.	Grade A, Level 1^+	55
75	In patients under the age of 80 years with good physical and mental status, systolic BP can be lowered to below 140 mmHg if treatment is well tolerated.	Grade B, Level 2^+	55
76	The management of hypertension in the elderly follows the same general guidelines, but begin drug treatment gradually, especially in the frail elderly. On starting drug treatment, carefully consider the patients' associated clinical conditions.	Grade A, Level 1^+	56

No.	Recommendation	Grade, Level of Evidence	CPG page no.
77	In elderly patients with isolated systolic hypertension, consider using calcium-channel blockers and diuretics.	Grade B, Level 2^{+}	56
78	In the elderly, measure the BP often in the supine (or sitting) position and standing position to detect a postural drop in the BP. Take care to avoid fluid depletion and electrolyte imbalance in the elderly.	GPP	56

Treatment of associated risk factors

	Recommendation	Grade, Level of evidence	CPG Page No.
79	Take into account the use of other drugs that decrease cardiovascular risk, such as lipid regulating drugs and antiplatelet drugs, in hypertensive patients with concomitant risk factors and increased cardiovascular risk.	Grade A, Level 1^{++}	57

Clinical quality improvement (Page 58)

The recommended target BP levels in antihypertensive treatment are:

1. Below 140/90 mmHg in patients aged under 80 years*
2. Below 150/90 mmHg in patients aged 80 years or more

*In elderly patients aged under 80 years with good physical and mental status if treatment is well tolerated.

The schedules shown in Table 8 (Page 44) are recommended to allow patients and healthcare providers to optimise the quality of care.

1 Introduction

1.1 Objectives and scope of guideline

The second edition of the MOH clinical practice guidelines on hypertension for Singapore was published in 2005. Since then, more facts about this important condition have emerged, particularly those recommending home blood pressure monitoring (HBPM) and 24-hour ambulatory blood pressure monitoring (ABPM) as key procedures in diagnosing suspected hypertension.

1.2 Target group

The main aim of these guidelines is to help physicians make sound clinical decisions about hypertension by presenting up-to-date information about diagnosis, classification, treatment, outcomes, and follow-up.

These guidelines are developed for all healthcare professionals in Singapore.

1.3 Guideline development

These guidelines have been produced by a MOH-appointed committee of cardiologists, internists, general medicine practitioners, renal physicians, family physicians and a neurologist. They were developed by the adaptation of existing guidelines, critical review of relevant literature and expert clinical consensus taking local practice into consideration. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or his guardian or carer.

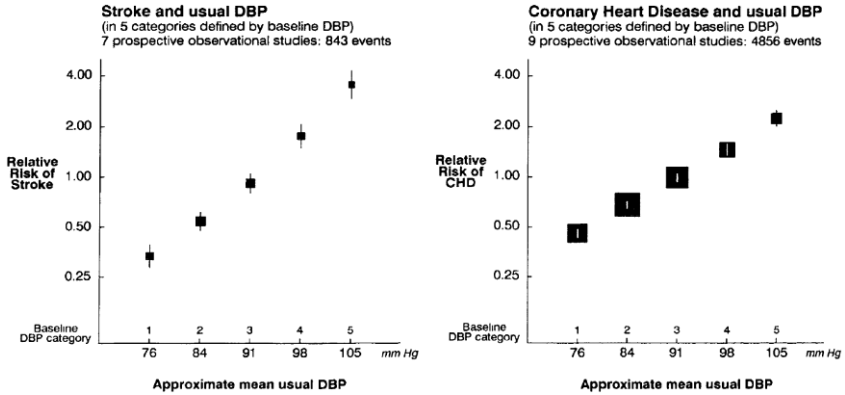
1.4 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or earlier if new evidence appears that requires substantive changes to the recommendations.

2 Epidemiology

Blood pressure (BP) levels are continuously related to the risk of cardiovascular disease as shown in Figure 1 below. The definition of hypertension or raised BP is therefore arbitrary.

Figure 1 Relative risk of cardiovascular disease in relation to patients' usual diastolic BP (square sizes proportional to numbers of events)



From MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, et al. Blood pressure, stroke, and coronary heart disease. The Lancet. 1990; 335:765-74.[1]

2.1 Epidemiology

The Singapore National Health Survey (NHS)[2] 2010 showed that the crude prevalence of hypertension (defined as BP of ≥140/90 mmHg) among Singapore residents aged 30 to 69 years was 23.5%, compared to 24.9% in 2004 and 27.3% in 1998. Of those aged between 18 to 69 years, close to 1 in 5 residents (18.9%) had hypertension in 2010.

In the NHS 2010, it was found that Malays (28.0%) had the highest prevalence of hypertension, followed by Chinese (23.4%) and Indians (19.3%). This result is in contrast to the NHS 2004, in which Chinese

(25.6%) persons had the highest prevalence of hypertension, followed by Malays (22.7%) and Indians (21.6%). Hypertension was more common among men (26.4%) than women (20.7%). The highest prevalence of hypertension among Singapore residents aged 30 to 69 years was in Malay women (29.8%), followed by Chinese men (27.2%) and Malay men (26.0%). The crude prevalence of hypertension by gender and ethnic group is shown in Figure 2 below.

The age-specific prevalence for hypertension rises markedly from age 40 years onwards. The age-specific prevalence of hypertension amongst those aged 60 to 69 years was 53.4% as compared to 7.6% in those aged 30 to 39 years.

Although infrequently, hypertension also occurs in younger individuals and children, many of whom have secondary hypertension. The NHS 2010 found that 3.3% of Singapore residents aged 18 to 29 years had hypertension, compared with 4.2% in 2004. In contrast, majority of adult hypertensive patients have primary hypertension (i.e. without any defined causes).

The NHS 2010 also found that the proportion of known hypertensive patients with good BP control (i.e. BP < 140/90 mmHg) was 67.4%, compared with 49.5% in 2004 as shown in Figure 3, while the proportion with good control among those receiving treatment was 69.1%, compared with 52.9% in 2004. In addition, 26.3% of those found to have hypertension in the NHS 2010 had not been previously diagnosed, compared with 38.5% in 2004.

Figure 2 **Crude prevalence (%) of hypertension among Singapore residents aged 30 to 69 years old, by gender and ethnic group, 2010**

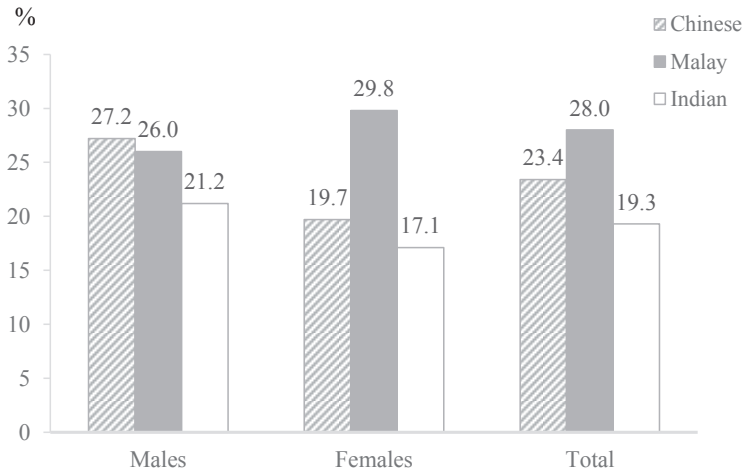
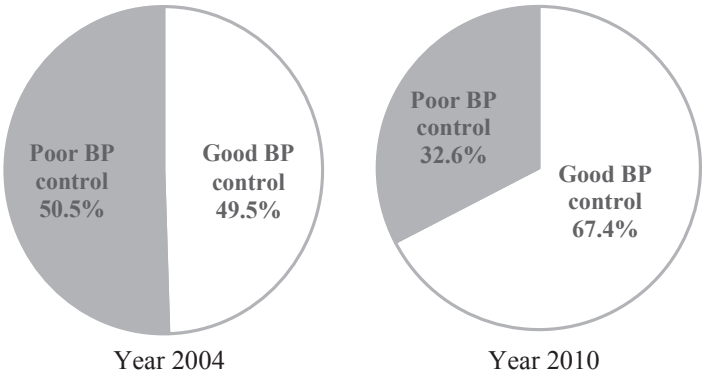


Figure 3 **Proportion (%) of patients with BP under control (< 140/90 mmHg) in 2004 and 2010**



3 Definition and classification of hypertension

As BP is characterised by large spontaneous variations, the diagnosis of hypertension should be based on multiple BP measurements taken on several separate occasions.

Definitions are given in Table 1 for subjects who are not taking antihypertensive medication and not acutely ill.[3]

Table 1 Definitions and classification of BP levels for adults aged 18 years and older

Category	Systolic BP	Diastolic BP
Normal BP	< 130 mmHg	< 85 mmHg
High-normal BP	130 to 139 mmHg	85 to 89 mmHg
Grade 1 hypertension	140 to 159 mmHg *	90 to 99 mmHg
Grade 2 hypertension	160 to179 mmHg *	100 to 109 mmHg
Grade 3 hypertension	≥ 180 mmHg *	≥ 110 mmHg
Isolated systolic hypertension	≥ 140 mmHg *	< 90 mmHg

* *Isolated systolic hypertension is graded according to the same level of systolic BP.*

D Classify hypertension according to systolic BP and diastolic BP levels.[3] When the systolic BP and the diastolic BP fall into different categories, the higher category applies.

Grade D, Level 4

For example, a BP of 162/92 mmHg is regarded as Grade 2 hypertension.

4 Measuring blood pressure

4.1 Clinic or office BP measurement

The BP is measured at rest several times on several occasions, with the patient in a supine or sitting position, using a non-invasive manometer, preferably an automated oscillometric device, validated according to standardised protocols and used in large BP studies across different populations. To ensure accuracy, non-mercury devices are periodically calibrated against values obtained simultaneously from a mercury sphygmomanometer, which itself has been calibrated and regularly serviced. When mercury devices become obsolete, periodic calibration will be done by the manufacturers of ocillometric devices.

Automated oscillometric devices remove the manual effort of cuff inflation, which can raise the BP to a misleading value,[3] and avoid missing the true systolic BP because a 'silent interval' sometimes occurs within the auscultatory method. Automation also promotes consistency and ease in HBPM; and produces greater accuracy if values are stored electronically.[3]

D Use the following procedures when recording BP:[3-6]

1. Allow the patient to sit or lie down for at least 3 minutes before measuring the BP.
2. The patient should refrain from smoking or taking caffeinated drinks during the 30 minutes before measurement.
3. Use a cuff with a bladder 12-13 cm x 35 cm in size. A cuff with a larger bladder should be used for large upper arms; where a thigh cuff should be used for extremely large arms.
4. When using the auscultatory method, use the disappearance of phase V Korotkoff sounds to measure the diastolic BP.
5. Measure the BP in both arms at the first visit; subsequently re-measure BP on the arm with the higher reading, if applicable.
6. Take 2 or more readings separated by 2 minutes. Average these two values. If the first two readings differ by 5 mmHg or more, further readings should be obtained and averaged.

7. In elderly subjects and diabetic patients, measure the BP in the supine (or sitting) position, and within 2 minutes after standing, to record any postural fall in BP.
8. Place the manometer cuff at the level of the heart, regardless the position of the patient.

Grade D, Level 4

4.2 Out of office BP measurement

Home and ambulatory BP

BP values obtained by HBPM, or by 24-hour ABPM are usually several mmHg lower than those obtained by clinic or office measurement. [3,7] Both HBPM and ABPM methods are valid, and moreover, the 24-hour average BP from ABPM independently and reliably predicts cardiovascular mortality.[3,8]

When measured in clinic or office, the alerting response in about 1 in 4 patients can result in exaggerated BP, leading to overdiagnosis of the disorder, or to the diagnosis of isolated clinic ('white-coat') hypertension.[3,9-11] Conversely, when a patient's clinic BP is normal but the out-of-clinic BP is raised, the condition is called isolated ambulatory or out-of-clinic hypertension ('masked' hypertension).[3]

D Wherever practicable, HBPM or ABPM (in that order) should be offered to younger patients, and to those whom target organ damage is found without a raised clinic BP. [3]

Grade D, Level 4

HBPM is cheaper, more widely available, easily repeatable, and shows day-to-day BP variability. Where affordable, HBPM can be offered to committed patients to boost treatment adherence via positive data feedback.

With HBPM, the BP should preferably be measured twice daily, in the morning and evening, adjusting for patients in long-term night-shift work. For each BP value in HBPM, at least two consecutive measurements are taken, 2 minutes apart and with the patient seated.[3,9] Additionally, BP should be measured over 4 to 7 (minimum 4) consecutive days. The HBPM mean is the average of BP values, counting from the 2nd monitoring day.[3,11]

C The preferred manometer is an automated oscillometric device, with or without memory.[11]

Grade C, Level 2+

HBPM yields many BP values over several days in the subject's usual environment.

D To ensure reliable values, the patient or carer needs training in device use, and a BP log-book (for basic devices without memory).[3]

Grade D, Level 4

24-hour ambulatory BP monitoring (ABPM) is the reference or 'gold standard' investigation, which records the BP during routine, day-to-day activities and during sleep, providing a measure of 24-hour BP variability. This is because a large body of BP information has been obtained previously using ABPM, across different subsets of patients, across different countries.

KEY RECOMMENDATION

GPP ABPM is recommended whenever in doubt about the diagnosis, e.g. to confirm borderline hypertension or abnormal results from HBPM.

GPP

GPP ABPM is also indicated for older, cognitively impaired, anxious or obsessive patients, in whom HBPM might be unreliable or inappropriate.

GPP

In borderline hypertension, ABPM can be repeated at intervals to support a definite diagnosis.[3,9,11] It is also used to optimise BP treatment to ensure BP levels are kept to the target range BP levels. Moreover, ABPM identifies patients with 'masked hypertension' ('isolated out-of-clinic hypertension') – in whom average BP is normal in the clinic but elevated at home and elsewhere.[3] Masked hypertension, often occurring in young obese men who smoke and drink excessively, is linked to a higher risk

of diabetes and chronic kidney disease.[3,11] The definitions of hypertension based on HBPM and ABPM are listed in Table 2.

Table 2 Definitions of hypertension in HBPM and ABPM

	Systolic BP	Diastolic BP
HBPM	≥ 135 mmHg	≥ 85 mmHg
ABPM		
• Daytime	≥ 135 mmHg	≥ 85 mmHg
• 24-hour	≥ 130 mmHg	≥ 80 mmHg
• Night-time	≥ 120 mmHg	≥ 70 mmHg

D Patients with an average BP ≥135/85 mmHg measured repeatedly at rest at home may be regarded as hypertensive.[3,9]

Grade D, Level 3

KEY RECOMMENDATION

D Patients with a 24-hour ABPM average BP ≥130/80 mmHg, or a daytime average BP ≥135/85 mmHg, or a night-time average BP ≥120/70 mmHg, are regarded as hypertensive.[3,9,10]

Grade D, Level 4

Table 3 Clinical indications for HBPM or 24-hour ABPM

Clinical indications for HBPM or 24-hour ABPM
1. Diagnosis of hypertension a) Borderline clinic BP b) Unusual variability of clinic BP
2. Suspicion of isolated clinic ('white coat') hypertension in subjects with low cardiovascular risk a) High clinic BP (grades 1&2) in individuals without target organ damage
3. Suspicion of isolated ambulatory (isolated out-of-clinic, or 'masked') hypertension a) Normal/high-normal clinic BP in individuals with target organ damage or at high total cardiovascular risk
4. Monitoring of the BP in treated hypertensive patients a) Identification of the excitatory (alerting) response ('white coat effect') to aid the monitoring of treated BP b) Patients with wide variability of clinic BP c) Suspicion of non-adherence to treatment d) Clinic BP not at target values after appropriate antihypertensive therapy e) Hypotensive symptoms after appropriate clinic BP and tailored antihypertensive treatment
5. Autonomic, postural, post-prandial, siesta- and drug-induced symptoms a) Symptoms suggesting hypotension from any likely cause, such as postural, autonomic, postprandial, afternoon nap-related, and drug-induced BP fall
6. Elevated clinic BP or suspected pre-eclampsia in pregnant women
7. Identification of true and false resistant hypertension
8. Other indications for 24-hour ABPM are a) Extreme discordance between clinic BP and home BP b) Assessment of within-day BP variability c) Evaluation of nocturnal BP dipping status
9. Suspicion of nocturnal hypertension, or absence of night-dipping, such as in patients with diabetes, chronic kidney disease, and obstructive sleep apnea syndrome, and in long-term night-shift workers

Adapted from the 2013 ESH/ESC Guidelines for the management of arterial hypertension.[11]

4.3 Central (aortic) BP

Central BP, measured by applanation tonometry and pulse-wave analysis, represents the haemodynamic load imposed on the heart, large arteries, and other target organs. The arterial pressure waveform includes the forward pulse wave-peak and a reflected wave-peak. Relating the pressure difference between these peaks to the pulse pressure yields an augmentation index, which predicts mortality from chronic kidney disease. Measuring central BP might reassure young patients with isolated systolic hypertension based on the brachial BP. However, central BP only adds slight prognostic value beyond brachial BP, and is unhelpful in most patients. The routine measurement of central BP is therefore premature.[3]

5 Evaluating high blood pressure

5.1 Aims of evaluation

The objectives of the clinical and laboratory evaluation of the hypertensive patient is to:

1. Determine the true BP level, and provide a definitive diagnosis of hypertension
2. Exclude or identify secondary causes of hypertension
3. Look for target-organ damage, and quantify its extent if present and
4. Identify other cardiovascular risk factors and clinical conditions that might influence the patient's treatment and prognosis

5.2 Clinical evaluation

D Routine clinical evaluation of a patient with elevated BP includes the following:[4,5,12]

1. Clinical and family history
2. Full standard physical examination
3. Laboratory investigations, including:
   a) Urine analysis: Dipstick for haematuria/albumin, microscopic examination, and test for albuminuria
   b) Measurement of serum concentrations of electrolytes, creatinine, urea, fasting glucose and fasting lipids
   c) Computation of estimated glomerular filtration rate (eGFR)
4. 12-lead electrocardiography (ECG)

Grade D, Level 4

Further tests should be guided by the history, physical examination and results of routine investigations. The tests aim to identify secondary causes of hypertension, in particular endocrine causes in younger subjects in the 2nd to 4th decades of life, and to obtain results which might significantly affect the patient's management. Such investigations include creatinine clearance, 24-hour urine content of protein, catecholamines and metanaphrines, serum uric acid and calcium levels, thyroid function indices, and the ratio of plasma levels of aldosterone to renin.[3]

Limited echocardiography could be conducted to confirm left ventricular hypertrophy (LVH) in patients whom examination or ECG, or both, suggest LVH.[3,9,10] Vascular ultrasonography used to detect aortic, carotid and peripheral arterial disease might also be necessary if clinically indicated.

In older patients, an unexpected or rapid BP reduction (> 20 mmHg systolic or > 10 mmHg diastolic BP)[3,9] after taking low doses of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) suggests high circulating levels of renin and angiotensin II. In this situation, look out for bilateral renal artery stenosis.[3,9,10]

The identifiable secondary causes of hypertension are listed in Table 4.

Table 4 Identifiable secondary causes of hypertension

Identifiable secondary causes of hypertension
1. Drug-related and substance-related* causes
2. Chronic kidney disease
3. Renal artery stenosis
4. Primary hyperaldosteronism
5. Hypercortisolism (Cushing's syndrome)
6. Phaeochromocytoma
7. Thyroid or parathyroid disease
8. Coarctation of the aorta
9. Obstructive sleep apnoea syndrome
10. Nephropathy from Type 1 diabetes mellitus
11. Rare monogenic ion transport disorders

* Several non-prescribed and illicit substances causes hypertension, e.g. liquorice, cocaine, amphetamine, crystal methamphetamine, and 3,4-methylenedioxy-methamphetamine (MDMA, 'Ecstasy')

6 Stratifying risk and approach to hypertension management

6.1 Risk assessment

KEY RECOMMENDATION

GPP Assess the overall cardiovascular risk and the patient's BP to guide the management of high BP.

GPP

Many methods of assessing overall cardiovascular risk exist, involving risk tables, charts or formulas, of which the Framingham Risk Score is the prototype risk scoring system.[13] The Framingham Risk Score has been modified locally, taking into account the Singapore cardiovascular epidemiological data in Singapore.[14]

D Refer to the locally adapted Framingham Risk Score to estimate cardiovascular risk.[13,14]

Grade D, Level 4

In individuals such as those with known or established coronary artery disease (CAD), other atherosclerotic vessel disease, diabetes mellitus, familial hypercholesterolemia, or malignant hypertension, the overall cardiovascular risk assessment is often unnecessary, as the risk is already high.

GPP Offer to start drug treatment immediately in patients with hypertension and existing high cardiovascular risk.

GPP

6.1.1 Prognostic factors

Prognostic factors consist of risk factors for cardiovascular disease, target organ damage, concomitant diseases such as renal disease, and other aspects of the patient's individual and medical circumstances (Table 5).

D Take the BP and other prognostic factors into account when deciding on the management of hypertensive patients.[15,16]

Grade D, Level 4

Table 5 Prognostic factors[5,17]

<table>
<tr><th colspan="2">Risk factors for cardiovascular disease</th></tr>
<tr><td colspan="2">1. Levels of systolic and diastolic BP (Grades 1&2)
2. Age (men ≥ 55 years; women ≥ 65 years)
3. Smoking
4. Family history of premature cardiovascular disease (men ≤ 55 years; women ≤ 65 years)
5. Dyslipidaemia
a) Total cholesterol > 6.2 mmol/L (240 mg/dL)
b) Triglycerides > 1.7 mmol/L (150 mg/dL)
c) HDL cholesterol < 1.0 mmol/L (40 mg/dL)
d) LDL cholesterol > 4.1 mmol/L (160 mg/dL)
6. Diabetes mellitus
7. Obesity (BMI ≥ 30 kg/m^2)
(BMI ≥ 27.5 kg/m^2)*</td></tr>
<tr><th colspan="2">Target organ damage (TOD) / associated clinical condition (ACC)</th></tr>
<tr><td>Cerebrovascular disease
1. Stroke (ischaemic or haemorrhagic)
2. Transient ischaemic attack</td><td>Renal disease
1. Albuminuria, at least moderately increased (ACR > 30 mg/mmol; PCR > 50 mg/mmol) or proteinuria (> 500 mg/24 hours)
2. Chronic kidney disease, at least stage 3 (eGFR< 60 ml/min)</td></tr>
<tr><td rowspan="2">Heart disease
1. Left ventricular hypertrophy (ECG, echocardiogram or chest X-ray)
2. Angina pectoris
3. Myocardial infarction
4. Coronary revascularisation
5. Congestive heart failure</td><td>Vascular disease
1. Aortic aneurysm
2. Peripheral arterial disease
3. Hypertensive retinopathy</td></tr>
<tr><td>Atherosclerosis
1. Ultrasound or radiological evidence of artherosclerotic plaque (carotid, iliac, femoral, peripheral arteries and aorta)</td></tr>
</table>

* Commensurate Asian body mass index (BMI) cut-point for action

6.2 Overall strategy

Patients' risk level for cardiovascular disease depends on BP and prognostic factors (see Table 6).[5,17]

Table 6 Risk stratification

BP Category	Prognostic factors			
	0-2 risk factors	≥ 3 risk factors	Established cardiovascular or renal disease	Symptomatic cardiovascular disease, chronic kidney disease stage ≥4 or diabetes with organ damage or risk factors
Grade 1 HT SBP 140-159 mmHg/ DBP 90-99 mmHg	Low risk			
Grade 2 HT SBP 160-179 mmHg/ DBP 100-109 mmHg		Medium risk		
Grade 3 HT SBP ≥180 mmHg/ DBP ≥110 mmHg	High or very high risk			

HT: Hypertension

A For high or very high risk individuals, begin immediate drug treatment for hypertension when other risk factors or conditions are present.[18]

Grade A, Level 1++

B For medium risk individuals, monitor the BP and other risk factors for several weeks, and obtain further information, before deciding whether to begin drug treatment.[19]

Grade B, Level 1+

B For low risk individuals, observe the patient over a significant period of time before deciding whether or not to begin drug treatment.[19]

Grade B, Level 1+

6.3 Benefits of treating hypertension

Evidence from a number of randomised controlled trials (RCTs) and meta-analyses show that the administration of BP-lowering drugs in hypertensive individuals decreases the risk of major clinical cardiovascular outcomes (i.e. fatal and nonfatal stroke, myocardial infarction, heart failure, and other cardiovascular deaths).[20-23] Based on meta-analyses of RCTs, antihypertensive treatment lowering diastolic BP by 5-6 mmHg reduced stroke incidence by more than 30%, and CAD by more than 14%.[20,21]

A sustained reduction of 12 mmHg in systolic BP over 10 years prevents:

1. 1 death per 11 patients with stage 1 hypertension and other cardiovascular risk factors and
2. 1 death per 9 patients in whom cardiovascular disease or target organ damage is present[4,24]

7 Treating high blood pressure

Good communication between the physician and the patient is core to the successful management of hypertension. Since the treatment of hypertension is for life, it is essential that the physician establishes a good professional relationship with the patient, provides the patient with information (both verbal and written), and answers any questions the patient might have.

Adequate information on the following is essential for satisfactory life-long control of hypertension:

1. BP monitoring
2. Risks assessment and prognosis
3. Target BP level
4. Lifestyle modification and
5. Expected benefits as well as the risks and side effects of treatment

A Wherever possible, use a team-based approach to manage a patient with hypertension, involving trained nurses and pharmacists with medical practitioners.[89]

Grade A, Level 1+

Hypertension, like many other chronic diseases, often requires a multidisciplinary approach involving clinicians who manage the majority of hypertensive patients, trained nurses (nurse clinicians), and pharmacists. A team-based approach with a disease management programme is associated with significantly improved BP control.[89,90]

Case management by nurse-led teams and interventions by pharmacists have been shown to improve medication adherence and to achieve higher proportions of BP targets reached. However, the delivery of the team-care service will depend on the local set-ups, availability of trained nurses and pharmacists, and cost-effectiveness.

7.1 Non-pharmacological therapy (Lifestyle modifications)

KEY RECOMMENDATION

A Recommend lifestyle changes to all hypertensive patients, and in patients with high normal BP. However, drug treatment should not be delayed without reason beyond 3 to 6 months if indicated.

Grade A, Level 1+

KEY RECOMMENDATION

A Advise patient to restrict salt intake to 5 to 6 g per day.[25-29]

Grade A, Level 1+

KEY RECOMMENDATION

A Moderate alcohol consumption to no more than 2 standard drinks per day for men, and to no more than 1 standard drink per day for women.[25,30,31,25-29]

Grade A, Level 1+

KEY RECOMMENDATION

A Increase the consumption of vegetables, fruits, low-fat dairy products, and decrease the intake of saturated and total fats.[25,32-37]

Grade A, Level 1+

KEY RECOMMENDATION

B Unless contraindicated, advise patients to reduce weight to a body mass index (BMI) below 23 kg/m^2 and to a waist circumference below 90cm in men, and below 80cm in women (for Asians).[38,39]

Grade B, Level 2+

KEY RECOMMENDATION

A Advise patients to do at least 30 minutes of moderate dynamic exercise 5 to 7 days per week.[25,40-42] Any physical exercise above the basal level, up to about 150 minutes a week, confers incremental cardiovascular and metabolic benefits, including BP reduction.

Grade A, Level 1+

KEY RECOMMENDATION

A Advise and offer assistance to all smokers to quit smoking.[43-45]

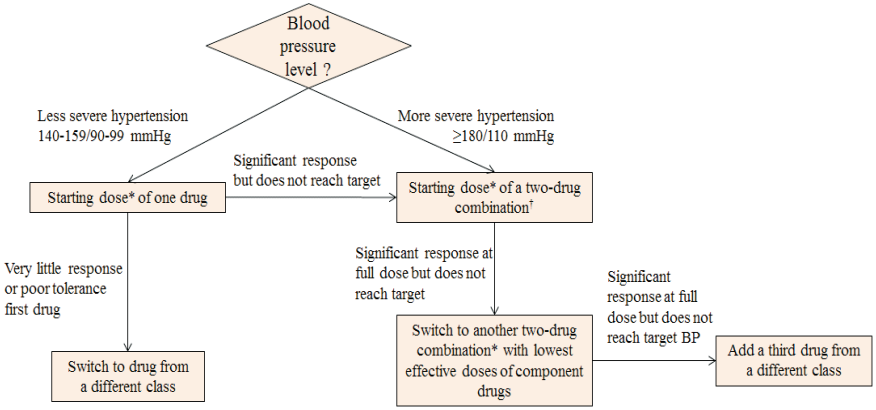
Grade A, Level 1+

7.2 Pharmacological treatment

7.2.1 Principles of drug treatment

Achieving target BP levels as rapidly as practicable is the most important principle of hypertension treatment.

Figure 4 Flowchart for drug treatment



*Start with the lowest effective dose

†Two-drug combinations may be either 2 separate drugs, or a fixed two-drug combination tablet.

B Begin appropriate combination treatment in patients whose pretreatment BP is raised (i.e. ≥ 140/90 mmHg), and specifically in patients whose BP is severely raised (≥ 180/110 mmHg), as they will require two or more drugs for adequate BP control.[3,9,47-49]

Grade B, Level 2+

D Initiate treatment at low doses, either singly or as a two-drug combination, to minimise side effects.[3,9-11]

Grade D, Level 4

A If an adequate dose of the first drug used demonstrated limited response or was poorly-tolerated, change to a different drug class instead of increasing the dose of the first drug.[47]

Grade A, Level 1+

The following principles may be applied when using antihypertensive drugs to lower BP regardless of the drug class:

1. Firstly, use low doses of drugs to initiate treatment, either singly or as a two-drug combination, starting with the lowest effective dose of a particular drug, to minimise side effects. Two-drug combination works faster in more severe hypertension, which might require 2 or even three drugs to attain target BP.[3,9-11]
2. If there is a significant response to a low dose of a single drug, but the BP is still above target BP, a low dose of a second drug from a different class should be added. Alternatively, the doctor may also increase the dose of the same drug if it is tolerated by the patient. Adding a low dose of a second drug, rather than increasing the dose of the original drug, confers advantages. This action allows both components to act at low doses, which are more likely to be free of side effects. The 2-drug combination also promotes the quicker attainment of BP targets. In this context, fixed low-dose combinations that are cheap should first be considered.
3. If taking a particular 2-drug combination does not reach target BP at full doses, then either switch to another 2-drug combination, starting with the lowest effective doses of the component drugs, or add a third drug from a different class.
4. Doctors should be aware that, in patients receiving long-term treatment, any change in drug dose or regimen takes full effect only

after 2-5 weeks, unlike the quicker BP changes in treatment-naïve patients.[46] Therefore, at least 2 weeks should pass before measuring the BP at the new steady-state, when titrating drug dosage or changing regimens, particularly in older patients.[46]

B Add a second drug when a single drug fails to achieve target BP.[47,48]

Grade B, Level 1+

Use of appropriate drug combinations maximises the BP lowering efficacy while minimising side effects. In most patients, appropriate combination treatment doubles the BP reduction compared to using single drugs (e.g. in patients with an initial BP of 160/100 mmHg, combination treatment reduces the BP to about 138/86 mmHg, compared to about 148/93 mmHg with a single drug).[47,48]

B Use long-acting drugs which provide 24-hour efficacy daily.[51]

Grade B, Level 2+

The advantages of long-acting drugs include better adherence to daily treatment, and smoother and more consistent control of the BP, i.e. reduced BP variability. The reduction in variability might confer greater protection against both the risk of major cardiovascular events, and the development of target organ damage.[50]

7.2.2 Choice of antihypertensive drugs

B In hypertensive patients without compelling indications or contraindications for any particular drug, consider any one, or any appropriate combination, of the five major pharmacological classes of antihypertensive drugs as the initial treatment.[3,9,10,73-75]

Grade B, Level 2++

A Take compelling indications and contraindications into account when prescribing an antihypertensive drug (Table 7).

Grade A, Level 1+

Table 7 Guidelines for selecting drug(s) for antihypertensive treatment

Concomitant conditions	Status	Drugs	Grade and level
Heart failure	Recommended	Diuretic,[3,10,11] ACE inhibitor,[52,53] ARB,[54] aldosterone antagonist (spironolactone, eplerenone),[3,9,10] or beta-blocker (bisoprolol, carvedilol)	Grade A, Level 1^{++}
	Supplementary treatment	Dihydropyridine calcium-channel blocker (amlodipine,[55,56] felodipine[57])	Grade C, Level 2^{+}
	Contraindicated	Non-dihydropyridine calcium-channel blocker (verapamil, diltiazem)[58]	Grade D, Level 4
Angina pectoris	Recommended	Beta-blocker[59] or dihydropyridine calcium-channel blocker[60]	Grade A, Level 1^{+}
Previous myocardial infarction	Recommended	Beta-blocker,[61] ACE inhibitor,[62] or ARB[63]	Grade A, Level 1^{++}
Atrial fibrillation, prevention	Recommended	Beta-blocker,[3,10,11] ACE inhibitor,[3] or ARB[3]	Grade B, Level 1^{+}
Atrial fibrillation, ventricular rate control	Recommended	Beta-blocker[3,11]	Grade A, Level 1^{+}
	Recommended	Non-dihydropyridine calcium-channel blocker[3,11]	Grade B, Level 2^{++}
Heart block	Contraindicated[†]	Beta-blocker,[3,11] or non-dihydropyridine calcium-channel blocker[3,11]	Grade B, Level 2^{++}
Peripheral artery disease	Recommended	ACE inhibitor[3] or dihydropyridine calcium-channel blocker[3]	Grade C, Level 2^{+}
Aortic aneurysm	Recommended	Beta-blocker[3]	Grade C, Level 2^{+}
Isolated systolic hypertension	Recommended	Diuretic,[3,64] or dihydropyridine calcium-channel blocker[55-57,65]	Grade A, Level 1^{+}
Diabetes mellitus	Recommended	ACE inhibitor[66] or ARB[67]	Grade A, Level 1^{+}
	Recommended	Dihydropyridine calcium-channel blocker[3,68]	Grade B, Level 2^{++}
	Supplementary treatment	Diuretic[3,68] or beta-blocker[3,11]	Grade B, Level 1^{+}

Table 7 Guidelines for selecting drug(s) for antihypertensive treatment (continue)

Concomitant conditions	Status	Drugs	Grade and level
Diabetes mellitus with albuminuria (moderately- or severely- increased albuminuria)	Recommended	ACE inhibitor[69] or ARB[70-72]	Grade A, Level 1^{+}
	Contraindicated	Any combination of ACE inhibitor with ARB	Grade A, Level 1^{+}
Previous stroke	Recommended	Any drug which effectively lowers the BP[3,11]	Grade A, Level 1^{++}
Asthma & chronic obstructive pulmonary disease	Contraindicated†	Beta-blocker[3,11]	Grade B, Level 2^{++}
Gout	Contraindicated†	Diuretic[3]	Grade C, Level 2^{+}
Bilateral renal artery stenosis	Contraindicated†	ACE inhibitor[3] or ARB[3]	Grade B, Level 2^{++}
Chronic kidney disease stage 5 (end-stage renal failure)	Recommended	ACE inhibitor[3] or ARB*[3]	Grade A, Level 1^{+}
	Contraindicated	Aldosterone antagonist[10]	Grade C, Level 2^{+}

*An ACE inhibitor should not be combined with an ARB in chronic kidney disease[3] (see page 51)
†Consider use of other first-line antihypertensive drug classes on page 38.

Some combination products might also cost less than the total cost of their separate components.

Selection of antihypertensive drug within the same class also depends on differences in cost and dosing frequency.

The choice of antihypertensive drug should be tailored to the individual patient, taking into account the following factors, in addition to risk profile and cost:[77]

1. Side effects
2. Drug-drug interactions
3. Patient preference

Begin first-line antihypertensive treatment with any one, or an appropriate combination, of the five major drug classes available in Singapore, namely:

1. Angiotensin-converting enzyme inhibitor (ACE inhibitor)
2. Angiotensin II receptor blocker (ARB)
3. Calcium-channel blocker (CCB)
4. Diuretic (thiazide, thiazide-like, or loop)
5. Beta-blocker

Other classes of antihypertensive drugs, such as methyldopa, hydralazine, and alpha-adrenergic receptor blockers (peripheral alpha-1 blockers such as terazosin; central alpha-2 blockers like clonidine) may be used in combination treatment as third or fourth-line agents.

D Be aware of the cost of treatment in selecting antihypertensive drugs.[77,78]

Grade D, Level 4

D Generic formulations, which usually cost less than newer non-generic (i.e. proprietary) drugs, are acceptable for use.[4]

Grade D, Level 4

C Do not offer aldosterone (mineralocorticoid) antagonists (e.g. spironolactone) to patients with chronic kidney disease, in particular when combined with an ACE inhibitor or ARB. This is because of the risks of further renal function impairment, and of hyperkalaemia.[3,9] An aldosterone antagonist might be considered in patients with resistant hypertension after a full work-up has excluded secondary hypertension (Table 4).[76]

Grade C, Level 2+

Recent RCT data indicate that the diuretic and beta-blocker combination drug produces metabolic changes which increase the risk of developing diabetes mellitus.[79]

B Prescribe a diuretic with caution as initial treatment in patients with uncomplicated hypertension, who are at risk for diabetes, because it might cause hyperglycaemia.[3,9,78]

Grade B, Level 2+

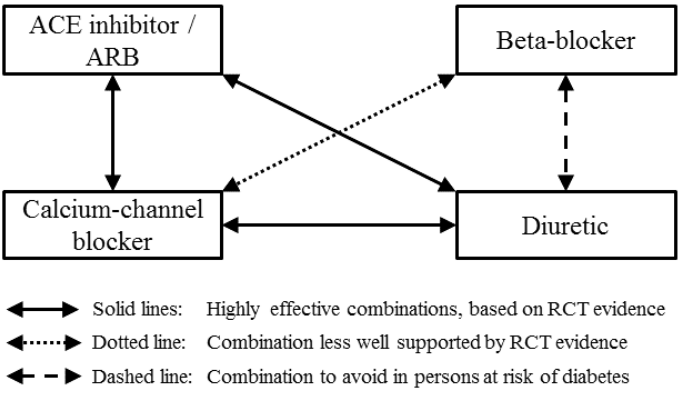
A Use beta-blockers with caution in patients at risk of developing diabetes, as it raises blood glucose concentrations.[79]

Grade A, Level 1+

7.2.3 Combination therapy

Figure 5 below summarises the pairing of the major drug classes.

Figure 5 Pairing the major drug classes



B Use the following drug combinations to treat hypertension[47]:

1. Calcium-channel blocker (dihydropyridine type) plus ACE inhibitor[81,82] or ARB[48]
2. Calcium-channel blocker plus diuretic[82]
3. Diuretic plus ACE inhibitor[47] or ARB[73]
4. Beta-blocker plus calcium-channel blocker (see caveat in Figure 5 above)[80]
5. Beta-blocker plus diuretic (see caveat in Figure 5 above)[47]

Grade B, Level 2^{++}

There is insufficient evidence that calcium-channel blocker plus ACE inhibitor or ARB combinations produce better cardiovascular outcomes than diuretic plus ACE inhibitor or ARB combinations.[3,83,84]

The beta-blocker and ACE inhibitor or ARB combinations do not produce synergistic reductions in the BP. The ACE inhibitor and ARB combination decreases glomerular filtration rate in patients with chronic kidney disease.[3,9]

B Avoid treating patients with an ACE inhibitor plus ARB combination, particularly patients who have chronic kidney disease.[3,9]

Grade B, Level 1^{+}

Although effective for lowering BP, the beta-blocker and diuretic combination increases the risk of developing diabetes mellitus.

B Beware of an increased risk of diabetes mellitus when offering a beta-blocker plus diuretic combination to patients with risk factors such as obesity or metabolic syndrome.[79]

Grade B, Level 2^{++}

7.3 Novel treatments in resistant hypertension

Resistant hypertension is defined as an average BP sustained at > 140/90 mmHg despite taking 3 antihypertensive agents at optimal tolerated doses, including a diuretic. When an aldosterone antagonist is used, it should be in patients with eGFR ≥ 45 ml/min, and closer monitoring of the renal function and serum electrolytes is needed if used in combination with an ACE inhibitor or ARB. Before diagnosing 'resistant hypertension', it is vital to exclude secondary causes of a raised BP (see Table 4, page 26).

Despite evidence of effectiveness based on an observational study (Symplicity HTN-1) and a randomised, non-sham-controlled study (Symplicity HTN-2), renal sympathetic denervation did not show effectiveness in a randomised, single-blind, sham-controlled trial (Symplicity HTN-3). Both the denervation group and control group showed a significant reduction in BP 6 months after the procedure (14.1 ±23.9 mmHg in the denervation group, versus 11.7 ±25.9 mmHg in the sham-procedure group) but there were no additional benefit of renal denervation.[85]

KEY RECOMMENDATION

A Do not offer renal sympathetic denervation for routine treatment of resistant hypertension.

Grade A, Level 1+

Prolonged bilateral activation of the carotid-sinus baroreceptor reflex (baroreflex) inhibits the adrenergic nervous system, thereby lowering the BP. Electrical stimulation of the baroreceptor reflex effectively decreases the BP for up to one year in patients with resistant hypertension.[86,87] However, the long-term efficacy and safety of carotid-sinus baroreceptor reflex activation is unknown. The technique is expensive and presently restricted to investigational use.

B Do not offer carotid-sinus baroreceptor reflex activation for routine treatment of resistant hypertension.[86-88]

Grade B, Level 2++

8 Treatment goals and follow up

8.1 Treatment goals

The primary treatment goal of a patient with hypertension is to achieve the maximum reduction in the total risk of cardiovascular disease. Apart from treating the raised BP, this goal requires the identification and treatment of all reversible risk factors, such as smoking, raised serum cholesterol, diabetes, and the management of associated clinical conditions.

The greater the risk profile, the more rigorous the BP control should be. For most patients, the goal of antihypertensive treatment should be to reduce the BP to < 140/90 mmHg.

A The recommended target BP treatment levels are:

1. BP < 140/90 mmHg in patients aged under 80 years[9]
2. BP < 150/90 mmHg in patients aged 80 years or older[9]

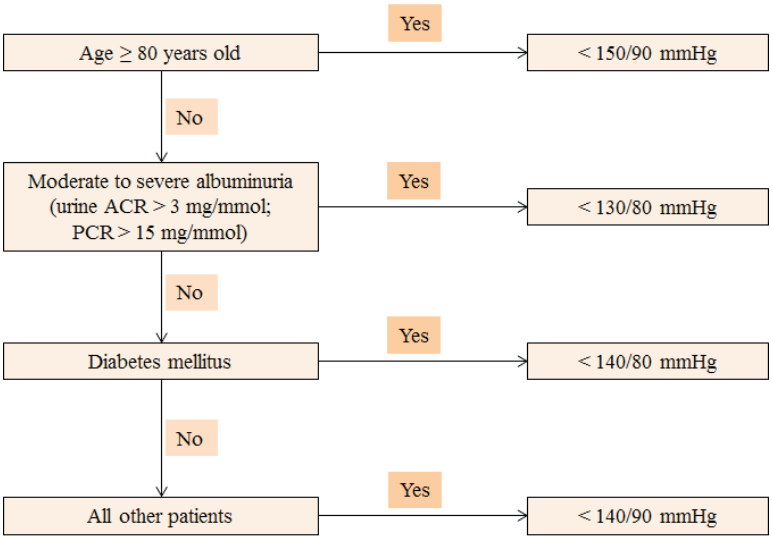
In fragile elderly individuals, the systolic BP goals should be adapted to individual tolerability.

Grade A, Level 1+

The BP level attainable with treatment is influenced by medication side effects and other co-morbidities, such as cerebrovascular disease. Good clinical judgment should therefore be exercised for every patient.

Figure 6 below summarises the clinic BP targets for different conditions.

Figure 6 Flowchart for clinic blood pressure targets



*If 2 conditions exist in the same patient, the condition that is mentioned first will determine the BP level.

†Clinic BP control should be optimised for individual patients to achieve the BP targets without worsening the eGFR and cardiovascular outcomes. Well patients above 80 years tolerating treated BP < 150/90 do not necessarily require treatment alteration. Home BP target will be the lower of either < 135/85 mmHg, or the clinic BP target as determined above.

8.2 Follow-up

Follow-up during evaluation and stabilisation of treatment should be sufficiently frequent to monitor the BP and other cardiovascular risk factors (Table 8, page 44).

C **Table 8 Frequency of recommended tests/actions**[4,5,12,77]

Recommended test/action	Recommended frequency
BP monitoring Risk level* - Low added risk - Medium to very high risk	 6-monthly to annually 3- to 6-monthly
BMI Fasting glucose Fasting lipid profile Serum electrolytes, urea, creatinine Urine-albumin measurement	Annually or more frequently, as per individual risk profile
ECG	As per individual risk and cardiac profile
Patient education Lifestyle modification and Medication adherence	At each visit

* Goal BP achieved.

Grade C, Level 2+

D Patients with the following problems should be referred to a hypertension specialist or clinic:[3]

1. Conditions needing emergency or urgent treatment, e.g. malignant hypertension, hypertensive heart failure, or other impending complications
2. Hypertension that is difficult to manage, e.g. unusually labile BP, or hypertension refractory to multiple drugs in different pharmacological classes
3. Secondary hypertension, i.e. hypertension due to an underlying cause, such as hyperaldosteronism
4. Hypertension in special circumstances, e.g. pregnancy, and young children.

Grade D, Level 4

9 Treating high blood pressure in special conditions

9.1 Type 2 diabetes mellitus

9.1.1 BP treatment targets

KEY RECOMMENDATION

B For patients with type 2 diabetes mellitus who have hypertension, an acceptable treatment target BP is below 140/80 mmHg. [91-93]

Grade B, Level 2+

KEY RECOMMENDATION

A Use ACE inhibitor, ARB, or calcium-channel blocker as first-line treatment in patients with diabetes without chronic kidney disease or proteinuria.[94-96]

Grade A, Level 1+

The new recommendation of BP range, < 140/80 mmHg for patients with type 2 diabetes mellitus, differs from the previous CPG's target BP of < 130/80 mmHg.

While BP-lowering treatment is strongly recommended in patients with diabetes when systolic BP is > 140 mmHg, the results from a 2011 meta-analysis of RCTs of BP targets in subjects with type 2 diabetes and impaired fasting glucose[91] suggest that most of the beneficial reduction in all-cause mortality in the intensive treatment group (systolic BP < 140 mmHg) occurred in trials in which the intensive group had achieved a systolic BP between 130 and 135 mmHg. For the outcomes of cardiovascular mortality, myocardial infarction and heart failure, although there was no statistical difference between the two groups, the point estimate favoured the intensive group, again mainly driven by trials which achieved a systolic BP between 130 and 135 mmHg. Neither the INVEST study nor the ACCORD study showed any improvement in cardiovascular outcomes in the intensive BP control

group (systolic BP < 130 mmHg in INVEST and < 120 mmHg in ACCORD), compared to the usual-control groups (systolic BP between 130 and 139 mmHg).[97,98] In the ACCORD trial, targeting systolic BP < 120 mmHg did not improve cardiovascular benefit, but there were significantly more adverse events, including hypotension and renal impairment.[98]

The meta-analysis results showed that, only for the outcome of stroke, the intensive treatment group with systolic BP ≤ 130 mmHg obtained greater benefit, compared to standard control group and the group treated to systolic BP between 130 and 135 mmHg.[91] Results from ACCORD and ONTARGET studies also showed improvement in stroke outcomes where the systolic BP was < 130 mmHg.[98,99]

Weighing the above evidence, it is reasonable to recommend, for most patients with type 2 diabetes, a target systolic BP between 130 and 139 mmHg.

Lower systolic BP targets might be appropriate in younger patients who are at low risk from the adverse consequences of achieving these targets. If a particular patient is at a greater risk for ischaemic stroke than for other cardiovascular outcomes, a lower systolic BP target of < 130 mmHg can be considered. [91] However, the risk of more adverse events with a lower BP target needs to be discussed with the patient.

In contrast, the existence of a J-curve has been investigated for diastolic BP, because a critical zone of diastolic BP is believed to be particularly important for maintaining coronary artery blood flow. The INVEST study showed that the hazard-ratio nadir in diastolic BP for both primary and secondary outcomes across age groups was between 70 and 80 mmHg.[93] Furthermore, an analysis of both the base-line and on-study BP in the VADT study subjects showed a higher risk for the primary composite cardiovascular end-point in patients with a diastolic BP lower than 70 mmHg.[92] Thus, based on current evidence, an acceptable target diastolic BP is <80 mm Hg.

9.1.2 Prioritising specific classes of antihypertensive drugs

In diabetic patients with severely-increased albuminuria (formerly 'macroalbuminuria'), hypertension is treated with an ACE inhibitor[11,69] or an ARB.[10,11,70-72] The two classes of renin-angiotensin-aldosterone (RAAS) blocker are also useful in patients with moderately-increased albuminuria (formerly 'microalbuminuria'), although the benefit of RAAS blockade on kidney disease progression in such patients is unproven.[11]

In patients without increased albuminuria,[3,10,11] monotherapy can start with an ACE inhibitor, ARB, calcium-channel blocker[68] (e.g. amlodipine), or a thiazide diuretic. Many experts, however, would select an ACE inhibitor or an ARB in these patients because these RAAS blockers can prevent albuminuria, while thiazide diuretics increase blood glucose levels (Table 7).

If 2 drugs are needed, combine a calcium-channel blocker with an ACE inhibitor. If an ACE inhibitor is not tolerated, then combine the calcium-channel blocker with an ARB.

9.1.3 Diabetic nephropathy

KEY RECOMMENDATION

A Optimised BP control is recommended to reduce the risk, or slow the progression, of diabetic nephropathy.[100,101]

Grade A, Level 1+

KEY RECOMMENDATION

A Treat patients with diabetic nephropathy to a target below 140 mmHg systolic BP.[97,98,102,103]

Grade A, Level 1+

KEY RECOMMENDATION

B If a diabetic nephropathy patient has severe albuminuria (equivalent to urinary albumin:creatinine ratio (ACR) more than 30 mg/mmol, or urinary PCR more than 50 mg/mmol), consider target below 130 mmHg systolic BP provided GFR changes are monitored carefully. [94,104,105]

Grade B, Level 2+

D Treat diabetic chronic kidney disease patients with moderate albuminuria (urinary ACR 3-30 mg/mmol, or urinary PCR between 15-50 mg/mmol) to a target BP equal to or below 130/80 mmHg.[106]

Grade D, Level 4

In patients with diabetes, large-scale randomised clinical trials have consistently shown the benefits of BP lowering on incident nephropathy, defined as the progression of albuminuria or worsening of serum creatinine, or both.[100,101]

There is sufficient evidence for lowering the BP below 140/90 mmHg in most patients with diabetic nephropathy. Recent evidence shows that BP lowering to < 130/80 mmHg in patients with diabetic nephropathy and pre-existing CAD is potentially harmful.[97,98,102,103] However, the recommendation to aim for a lower BP of < 130/80 mmHg in diabetic nephropathy patients with severe albuminuria (equivalent to urinary ACR more than 30 mg/mmol, or urinary PCR more than 50 mg/mmol) was supported by a RCT.[102] To decrease the risk or slow the progression of nephropathy, a BP target of < 130/80 mmHg appears reasonable.

When moderate to severe albuminuria is present, systolic BP values < 130 mmHg can be pursued, aiming to slow the progression of kidney disease, provided that changes in eGFR are monitored. The evidence for this recommendation is extrapolated from RCTs and from a systematic review of patients with non-diabetic nephropathy.[94,104,105] There are insufficient RCT data to specify a diastolic BP target.

However, the extent of BP reduction, intending to retard the progression of diabetic nephropathy, needs to be weighed against potential cardiovascular harms in high-risk patients.

KEY RECOMMENDATION

A Use an ACE inhibitor or ARB as first-line treatment, whenever treatment with BP-lowering drugs is indicated in diabetic nephropathy.[94-96]

Grade A, Level 1+

KEY RECOMMENDATION

D In diabetic nephropathy, if one class of RAAS blocker (either ACE inhibitor or ARB) is not tolerated, replace it with the other class.[50]

Grade D, Level 4

KEY RECOMMENDATION

A Combination treatment with both an ACE inhibitor and an ARB should not be routine in diabetic nephropathy.[107,108]

Grade A, Level 1+

KEY RECOMMENDATION

D When ACE inhibitors, ARBs, or diuretics are used in diabetic nephropathy, it is recommended to monitor the serum creatinine and potassium levels for the possible development of acute kidney injury and hyperkalemia.[50]

Grade D, Level 4

A Beta-blockers, calcium-channel blockers, and thiazides are all appropriate second-line therapy in diabetic nephropathy.[97-99, 50]

Grade A, Level 1+

BP control in diabetic nephropathy often requires combination therapy. Due to the greater effect of RAAS blockers on urinary protein excretion, the combination is recommended to include either an ACE inhibitors or an ARB. Although concurrent administration of an ACE inhibitor and an ARB can further decrease proteinuria, prescribing two RAAS blockers together cannot be routinely recommended in high-risk patients because of the increased risks of hyperkalemia and renal dysfunction, as reported in ONTARGET.[107,108]

Thiazide and thiazide-like diuretics are often used together with an RAAS blocker to control the BP and to attenuate hyperkalemia. Calcium-channel blockers have been shown to be useful, especially when combined with RAAS blocker. The non-dihydropyridine calcium blockers, verapamil and diltiazem, have consistently greater anti-proteinuric effects in protein-leaking patients compared to dihydropyridine CCBs, according to a meta-analysis of 28 randomised trials.[108] The likely explanation lies in the different efficacies of the non-dihydropyridine and dihydropyridine blockers in altering the autoregulation of renal blood flow. However, in practice, so long as the calcium-channel blocker is used together with either an ACE inhibitor or an ARB, the difference in protein excretion between calcium-channel blocker subclasses vanishes.

9.2 Non-diabetic chronic kidney disease

Hypertension is a risk factor for the development and progression of chronic kidney disease. Conversely, chronic kidney disease is a major risk factor for cardiovascular disease. Treating hypertension can slow the progression of proteinuric chronic kidney disease (moderate to severe albuminuria equivalent to urinary ACR more than 3 mg/mmol, or urinary PCR more than 15 mg/mmol) and reduce the rate of cardiovascular complications.

RCTs suggest that BP maintained at or below 130/80 mmHg retards the progression of proteinuric chronic kidney disease.[94-96]

Both ACE inhibitors and ARBs have been shown to decrease urinary albumin levels. In RCTs in patients with severely-increased albuminuria, both ARBs and ACE inhibitors significantly lower the risks of adverse renal outcomes.[94-96]

A Treat non-diabetic, non-proteinuric chronic kidney disease patients to a target BP below 140/90 mmHg.[94-96]

Grade A, Level 1+

KEY RECOMMENDATION

A Treat non-diabetic chronic kidney disease patient with severe albuminuria to a target BP equal to or below 130/80 mmHg.[94-96]

Grade A, Level 1+

D Treat non-diabetic chronic kidney disease patients with moderate albuminuria to a target BP equal to or below 130/80 mmHg.[106]

Grade D, Level 4

KEY RECOMMENDATION

A Use either an ACE inhibitor or an ARB as the first-line drug whenever treatment with BP-lowering drugs is indicated in non-diabetic chronic kidney disease patients.[94-96]

Grade A, Level 1+

A Combination treatment with both an ACE inhibitor and an ARB should not be routinely prescribed in non-diabetic chronic kidney disease patients.[94-96]

Grade A, Level 1+

9.3 Heart failure

Heart failure with reduced ejection fraction

Beta-blockers are useful for BP control in combination therapy, in particular in patients with CAD and heart failure. In patients with systolic heart failure (also known as heart failure with reduced ejection fraction), the appropriate BP lowering drug classes are ACE inhibitor,[52] ARB,[54] beta-blocker,[3,11] and aldosterone antagonist,[10,11] or appropriate combinations thereof which improve survival (Table 7). Diuretics, including loop diuretics (e.g. furosemide, bumetanide) or thiazide/thiazide-like drugs are given to relieve heart-failure symptoms and fluid retention.[10] An ACE inhibitor or ARB, or a beta-blocker is particularly useful in hypertensive patients with atrial fibrillation.[11] A beta-blocker is also helpful in those with exertional angina.[60]

Of the dihydropyridine calcium-channel blockers, amlodipine[55,59] and felodipine[56] are well tolerated in systolic heart failure, but should probably constitute supplementary treatment, because they do not increase survival, effort tolerance, or the quality of life.[55,57,59] Non-dihydropyridine calcium-channel blockers increase the risk of worsening HF and of hospital care therefrom.[58]

9.4 Stroke

9.4.1 Lowering of the BP in acute stroke

Both extremely high and extremely low BP are associated with poor outcomes during the early phase of acute ischaemic stroke.[110-116] A high BP decreases spontaneously by about 20/10 mmHg in patients with acute ischaemic stroke within the first ten days of hospital stay.[113]

KEY RECOMMENDATION

A Where systolic BP is above 140 mmHg but below 220 mmHg within the first two weeks of onset of acute ischaemic stroke, lowering of high BP should be based on individual clinical judgment after careful consideration of all the contraindications.[114-119]

Grade A, Level 1^{++}

According to randomised trials, the lowering of high BP with antihypertensive drugs within the first two weeks after the onset of acute stroke does not significantly improve the functional outcome.[113-118] Generally, the patients who were enrolled in these trials had mild stroke, and patients with severe cerebrovascular stenosis and impaired consciousness were usually excluded.

KEY RECOMMENDATION

D It is reasonable to lower, with care, a markedly elevated BP (systolic BP above 220 mmHg or diastolic BP above 120 mmHg, or both) by 10% to 15% during the first 24 hours after the onset of acute ischaemic stroke.[120]

Grade D, Level 4

During the first 24 hours after stroke onset, a targeted reduction in BP by 10%-15% from base-line pressure is inadequate for a stroke patient who has received a fibrinolytic (thrombolytic) agent, or who has hypertensive encephalopathy, aortic dissection, acute renal failure, acute myocardial infarction, acute pulmonary oedema, or any combination thereof. In stroke patients with these comorbidities, their BP can be lowered more rapidly to below 180/110 mmHg if their initial systolic BP > 220 mmHg or diastolic BP > 120 mmHg, before specific treatment begins.[121] The rate of BP reduction would depend on the specific comorbidities.

9.4.2 Lowering of the BP after transient ischemic attack and after acute phase of stroke

KEY RECOMMENDATION

D After the acute phase of stroke, begin antihypertensive treatment in hypertensive patients if the systolic BP is more than 140 mmHg and diastolic BP is more than 90 mmHg.[122,123]

Grade D, Level 4

KEY RECOMMENDATION

A Use any of the five major pharmacological classes of antihypertensive drugs for stroke prevention in patients after the acute phase of stroke, provided that the BP is effectively lowered.[21,75]

Grade A, Level 1++

GPP The target BP level in patients after transient ischemic attack and after acute phase stroke should be individualised, with careful consideration of medical comorbidities. A lower systolic BP target might benefit a patient who has small vessel disease, but might harm a patient with severe cerebrovascular stenosis.

GPP

The lowering of the BP with antihypertensive drugs after the acute phase of stroke in both normotensive and hypertensive patients decreases recurrent stroke and other vascular events.[123] Some international guidelines recommend beginning treatment for patients with ischaemic stroke, in whom the systolic BP is > 140 mmHg and diastolic BP is > 90 mmHg.[122,123]

A reduction of 10/5 mmHg from base-line BP has been shown to prevent vascular events in stroke patients.[124] The absolute target BP level is uncertain. There is preliminary evidence showing that a lower systolic BP benefits patients with stroke which is due to small vessel disease,[125] but harms those with stroke associated with severe cerebrovascular stenosis.[126,127] Meta-analyses of RCTs suggest that all five major pharmacological classes of antihypertensive drugs are appropriate for stroke prevention, provided that the BP is effectively decreased.[21,75] (see 7.2.2 above)

9.5 Pregnancy

Hypertension in pregnancy is defined by a systolic BP of 140 mmHg or greater, diastolic BP of 90 mmHg or greater, or both. High BP before pregnancy or that which occurs in the first half of pregnancy is called chronic (primary) hypertension. Primary care physicians should refer to specialist for treatment in pregnancy if hypertension is classified as chronic hypertension with superimposed preeclampsia, preeclampsia/eclampsia and gestational hypertension.

D Even though the classification of mild, moderate and severe hypertension by BP level is different in pregnancy, pharmacological treatment is recommended in pregnant women with chronic hypertension who have a persistently elevated systolic BP of 150 mmHg or greater, or a diastolic BP of 100 mmHg or greater.[128]

Grade D, Level 4

GPP Avoid aggressive rates of lowering of BP in pregnant women with chronic hypertension, because of the potential risk of compromising the uteroplacental blood flow.

GPP

D In pregnant women with no target organ damage, and uncomplicated chronic hypertension, aim to keep the BP below 150/100 mmHg.[128]

Grade D, Level 4

D In pregnant women with target organ damage secondary to chronic hypertension, aim to keep the BP below 140/90 mmHg.[128]

Grade D, Level 4

D In pregnant women with uncomplicated chronic hypertension, do not use drug treatment to decrease the diastolic BP to below 80 mmHg.[128]

Grade D, Level 4

D Treat pregnant women with chronic hypertension using methyldopa, labetalol, nifedipine, or a combination thereof.[128]

Grade D, Level 4

GPP Methyldopa, labetolol, and nifedipine are also considered safe for use during breastfeeding postpartum.

GPP

Diuretics of all types are less often used during pregnancy, because of possible concerns about depletion of the intravascular volume; they might also reduce the quantity of milk production postpartum. In particular, for hydrochlorothiazide, there might be an increased risk of congenital abnormality and neonatal complications if taken during pregnancy.[128]

D ACE inhibitors, ARBs, direct renin inhibitors (e.g. aliskiren), and aldosterone antagonists should be avoided during pregnancy.[128]

Grade D, Level 4

9.6 Elderly patients

KEY RECOMMENDATION

A In elderly hypertensive patients whose systolic BP is 160 mmHg or higher, the BP should be reduced to below 150/90 mmHg.[3,10,11,37,129]

Grade A, Level 1+

B In patients under the age of 80 years with good physical and mental status, systolic BP can be lowered to below 140 mmHg if treatment is well tolerated.[3,10,11]

Grade B, Level 2++

An elevated systolic BP is common in the elderly, and is termed isolated systolic hypertension. Arterial compliance decreases with advancing age, and this change produces a gradual rise in the systolic BP and a fall in the diastolic BP. A wide pulse pressure is strongly associated with an increase in cardiovascular and cerebrovascular events,[20,130] and with heart failure.[131]

RCTs have shown the benefits of treating isolated systolic hypertension across a wide age range.[129] In patients over the age of 80 years, a recent meta-analysis of antihypertensive drug treatment concluded that combined fatal and non-fatal cardiovascular events decreased significantly, but all-cause mortality did not.[132]

KEY RECOMMENDATION

A The management of hypertension in the elderly follows the same general guidelines, but begin drug treatment gradually, especially in the frail elderly. On starting drug treatment, carefully consider the patients' associated clinical conditions.[68,72,133-135]

Grade A, Level 1+

Various classes of drugs (ACE inhibitors, ARB, beta-blockers, calcium-channel blockers and diuretics) have been shown in RCTs to be effective and beneficial in elderly patients.[68,72,133-135]

KEY RECOMMENDATION

B In elderly patients with isolated systolic hypertension, consider using calcium-channel blockers and diuretics.[68,72,133-135]

Grade B, Level 2+

Similar to other patients, many elderly patients require two or more antihypertensive drugs to achieve good BP control. Consistent control of the diastolic BP is difficult, and the optimum range of the treated diastolic BP needs further clarification. The current impression is that the diastolic pressure should not be allowed to fall below 60 mmHg, particularly in those with known CAD, because impaired coronary artery filling at extremely low BP levels might increase the risk of coronary events.

KEY RECOMMENDATION

GPP In the elderly, measure BP often in the supine (or sitting) position and standing position to detect a postural drop in the BP. Take care to avoid fluid depletion and electrolyte imbalance in the elderly.

GPP

10 Treatment of associated risk factors

Cholesterol lowering and antiplatelet therapy

A Take into account the use of other drugs that decrease cardiovascular risk, such as lipid regulating drugs and antiplatelet drugs, in hypertensive patients with concomitant risk factors and increased cardiovascular risk.[19, 136]

Grade A, Level 1^{++}

In patients with high serum cholesterol level, there are benefits for cholesterol lowering treatment regardless of the BP level. Therefore, the use of lipid regulating drugs is recommended for hypertensive patients who have elevated serum cholesterol levels, aiming in particular to decrease serum low-density lipoprotein cholesterol.[12]

In patients with a history of CAD or cerebrovascular disease, there is evidence that aspirin and some other antiplatelet agents (e.g. clopidogrel, prasugrel, and ticagrelor) can decrease cardiovascular risks.[4,19,137] Antiplatelet drug treatment should also be considered in some patients in the high risk categories (Table 6, page 29) who already have satisfactory BP control.

11 Clinical quality improvement

The recommended target BP levels in antihypertensive treatment are

- Below 140/90 mmHg in patients aged under 80 years*[9-11]
- Below 150/90 mmHg in patients aged 80 years or more[10,11]

*In elderly patients aged under 80 years with good physical and mental status, if treatment is well tolerated.

The ultimate objective of managing hypertension is not to lower the BP *per se*, but to decrease the patients' overall risks of morbidity and mortality. These risks are also influenced by other coexisting cardiovascular disease risk factors. The greater the total cardiovascular disease risk, the more rigorously the BP should be controlled.

However, the BP level attainable with antihypertensive treatment is influenced by medication side effects and other comorbidities, such as diabetes, chronic kidney disease, CAD, and cerebrovascular disease. Good clinical judgment should therefore be exercised in every patient.

The schedules shown in Table 8 (page 43) are recommended to allow patients and healthcare providers to optimise the quality of care.

Each patient should be managed appropriately according to their assessed risk level.

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category 3A (Self-Study) of the SMC Online CME System. Alternatively, you can claim one CME point under Category 3B (Distance Learning – Verifiable Self-Assessment) if you answer at least 60% of the following MCQs correctly. You can submit your answers through the SMJ website at this link: http://sma.org.sg/publications/index.aspx?ID=26 (the link will only be available once the January 2018 issue of the SMJ becomes available). The answers will be published in the SMJ March 2018 issue and at the MOH webpage for these guidelines after the period for submitting the answers is over.

Instruction: Choose True or False for each statement.

		True	False
1.	With regards to diagnosis of hypertension		
	A. Patients with a 24-hour ABPM are regarded as hypertensive if the average BP is ≥135/85 mmHg.	☐	☐
	B. It has been estimated that antihypertensive treatment, on average, reduces stroke by 35-40%	☐	☐
	C. If BP 165/95 mmHg we should grade the hypertension as Grade 2.	☐	☐
	D. The cardiovascular risks rise exponentially for BP between 140/90 and 220/120 mmHg; the urgency of treatment is therefore guided by the grade of measured BP.	☐	☐
2.	With regards to evaluation and prognostic factors of hypertension,		
	A. One of the objectives of the clinical and laboratory evaluation of the hypertensive patient is to look for target organ damage.	☐	☐
	B. Urine analysis should be part of routine clinical evaluation.	☐	☐
	C. Central aortic pressure should be part of routine evaluation in a hypertensive patient.	☐	☐
	D. Chronic sleep deprivation syndrome is a common secondary cause of hypertension	☐	☐

3. With regards to lifestyle modifications and non-pharmacotherapy,

A. Salt (sodium chloride) restriction up to 5-6 g a day is strongly recommended in those with hypertension. ☐ ☐

B. Regular dynamic (ie aerobic) exercise on at least 5 days a week, whether as single or interrupted episodes of 30 minutes or longer, confers both cardiovascular and overall health benefits, beyond a reduction in the BP. ☐ ☐

C. Lifestyle modifications are not required in patients whose average BP is in the high normal range of 130-139 / 85-89 mmHg. ☐ ☐

D. Cessation of tobacco smoking confers major benefit in terms of BP reduction, as well as avoiding coronary artery disease and other serious systemic disorders. ☐ ☐

4. The following two-drug antihypertensive combinations decrease the BP (BP) beyond the amount obtained by adding together the individual drug effects on the BP:

A. Atenolol plus lisinopril. ☐ ☐

B. Amlodipine plus valsartan. ☐ ☐

C. Carvedilol plus indapamide. ☐ ☐

D. Enalapril plus losartan. ☐ ☐

5. With regards to treatment in various conditions:

A. In treatment of Type 2 diabetes mellitus, an acceptable treatment-initiation and target BP is < 140/80 mmHg. ☐ ☐

B. In lowering of BP for secondary prevention of stroke, the threshold for starting anti-hypertensive therapy is > 140/90 mmHg. ☐ ☐

C. In treatment during pregnancy, initiation of pharmacological treatment is recommended for pregnant women with chronic hypertension if the BP is more than 140/90 mm Hg. ☐ ☐

D. Elderly patients above age 80years with isolated systolic hypertension should have their systolic BP reduced to < 140mmHg. ☐ ☐

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