Guidelines

The 2012 Canadian Hypertension Education Program
Recommendations for the Management of Hypertension:
Blood Pressure Measurement, Diagnosis, Assessment of
Risk, and Therapy

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See page 285 for disclosure information.

A version of the hypertension recommendations designed for patient and public education has been developed to assist health care practitioners managing hypertension. The summary is available electronically (go to http://www.hypertension.ca or http://www.heartandstroke.ca).
We updated the evidence-based recommendations for the diagnosis, assessment, prevention, and treatment of hypertension in adults for 2012. The new recommendations are: (1) use of home blood pressure monitoring to confirm a diagnosis of white coat syndrome; (2) mineralocorticoid receptor antagonists may be used in selected patients with hypertension and systolic heart failure; (3) a history of atrial fibrillation in patients with hypertension should not be a factor in deciding to prescribe an angiotensin-receptor blocker for the treatment of hypertension; and (4) the blood pressure target for patients with nondiabetic chronic kidney disease has now been changed to < 140/90 mm Hg from < 130/80 mm Hg. We also reviewed the recent evidence on blood pressure targets for patients with hypertension and diabetes and continue to recommend a blood pressure target of less than 130/80 mm Hg.
Executive Summary

Objective: To update the evidence-based recommendations for the prevention, diagnosis, assessment, and treatment of hypertension in adults for 2012.

Options and Outcomes: For lifestyle and pharmacologic interventions, randomized trials and systematic reviews of trials were preferentially reviewed. Changes in cardiovascular morbidity and mortality, as well as total mortality were the primary outcomes of interest. However, for lifestyle interventions, blood pressure lowering was accepted as a primary outcome, and progressive renal impairment was also accepted as a clinically relevant primary outcome among patients with chronic kidney disease.

Evidence: A Cochrane Collaboration librarian conducted an independent MEDLINE search up to August 2011 to update the 2011 recommendations. To identify additional studies, reference lists were reviewed and experts were contacted. All relevant articles were reviewed and appraised independently by both content and methodology experts using prespecified levels of evidence.

Recommendations

Diagnosis and assessment

A new recommendation this year relates to the diagnosis of white coat hypertension, which could be confirmed either by reliable repeated home blood pressure (BP) monitoring or 24-hour ambulatory BP monitoring (ABPM). Recommendations for BP measurement, criteria for hypertension diagnosis and follow-up, assessment of global cardiovascular risk, diagnostic testing, diagnosis of renovascular and endocrine causes of hypertension, ambulatory monitoring, and the use of echocardiography in hypertensive individuals are unchanged.

Prevention and treatment

New recommendations include: (1) aldosterone antagonists are recommended for hypertension and systolic heart failure in addition to the suggested therapy; (2) a history of atrial fibrillation (AF) in patients with hypertension should not be a factor in deciding to prescribe an angiotensin-receptor blocker (ARB) for the treatment of hypertension; (3) from a reevaluation of the evidence, BP targets for patients with nondiabetic chronic kidney disease (CKD) is now <140/90 mm Hg instead of <130/80 mm Hg; (4) The BP target for patients with hypertension and diabetes mellitus did not change (<130/80 mm Hg) based on evaluation of recent meta-analyses. Recommendations on lifestyle modifications to prevent and treat hypertension, indications for pharmacologic management of hypertension, treatment thresholds and targets, choice of therapy for adults with hypertension and without compelling indications for other agents, isolated systolic hypertension, cerebrovascular disease, proteinuric nondiabetic CKD, ischemic heart disease, left ventricular hypertrophy, diabetes, and global vascular protection have not changed. Treatment for pheochromocytoma, primary hyperaldosteronism, and strategies to improve antihypertensive medication adherence are unchanged.

Validation

All recommendations were graded according to the strength of the evidence and voted on by the 65 members of the Canadian Hypertension Education Program (CHEP) Recommendations Task Force. All recommendations reported herein achieved at least 80% consensus. CHEP will continue to update recommendations annually. All recommendations are outlined in this document.

Introduction

Hypertension affects 27% of the Canadian adult population aged 35-64 years and over 50% of people aged 65 years and older. hypertension remains one of the most common modifiable risk factors for cardiovascular disease in Canada and globally. Each year, numerous studies are published that may affect the clinical practice of hypertension. The objective of the annual updates on the CHEP recommendations is to provide timely evidence-based recommendations to primary care providers to improve hypertension prevention, detection, and control in Canadians. Key clinical questions addressed include: (1) How is hypertension diagnosed? (2) How do we diagnose white coat hypertension? (3) What frequency of follow-up and laboratory testing is necessary for hypertensive patients? (4) How is risk assessed for future cardiovascular events in these patients? (5) When should we start pharmacological therapy to control hypertension? (6) What BP level should be attained in hypertensive patients and in patients with coexisting diabetes or CKD? (7) What lifestyle interventions are effective in preventing hypertension and reducing BP? (8) What are the optimal pharmacological agents for treatment of hypertension, as well as hypertension occurring in patients with specific comorbid conditions, including diabetes, cardiovascular disease, stroke, or kidney disease? (9) How can we improve adherence to antihypertensive medications? (10) How do we diagnose and treat secondary causes of hypertension, renovascular hypertension, pheochromocytoma, and hyperaldosteronism?

In this document, we outline all of the recommendations and discuss the evidence and rationale on those recommendations that are new or updated. More detailed discussion of previous changes to the Canadian recommendations is available in prior publications. This year, the recommendations underwent significant revision based on recently published trials and reevaluation of earlier studies: Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (EMPHASIS-HF) trial, Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS), and Randomized Aldactone Evaluation Study (RALES) for the heart failure recommendation; Attrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events (ACTIVE I), Angiotensin II Antagonist in Paroxysmal Atrial Fibrillation (ANTIPAF) and Gruppo Italiano per lo Studio della Sopravvivenze nell’Infarto Miocardico-Atrial Fibrillation (GISSI-AF) for AF; African American Study of Kidney Disease and Hypertension (AASK) follow-up extension trial, Ramipril Efficacy in Nephropathy-2 (REIN-2), and Modification of Diet in Renal Disease (MDRD) trials for the BP targets for CKD; and 2 meta-analyses of large clinical trials recently published on BP treatment targets for patients with diabetes. Also, the evidence base for diagnosing white coat hypertension using home BP monitoring was reviewed.

These recommendations are targeted toward primary care providers and apply to adults at risk for or with hypertension. For issues related to the diagnosis and evaluation of high BP in children and adolescents, the reader is referred to separate guidelines. A version of the hypertension recommendations...
designed for patient and public education has been developed to assist health care practitioners managing hypertension. The summary is freely available at: http://www.hypertension.ca.

Although we mention individual antihypertensive agents when discussing trials, the reader may assume that all drug-specific recommendations are applicable to the entire drug class in question, unless otherwise stated. Finally, although these recommendations are based on best evidence, health care providers must also use their own clinical judgement and consider patient preferences when applying these recommendations for their patients.

Methods

A Cochrane Collaboration librarian conducted a MEDLINE/PubMed search using text words and MeSH headings (copies of the different strategies are available upon request). Common search terms were hypertension[MeSH], hypertens*[ti, ab], and blood pressure, which were then combined with terms for the specific concept each subgroup investigated. A highly sensitive search strategy for randomized trials and systematic reviews published up to August 2011 was used, and in order to ensure that all relevant studies were included, bibliographies of identified articles were also manually searched (details of search strategies and retrieved articles are available on request). Studies were selected if they included the relevant outcomes. The outcomes primarily considered included changes in cardiovascular morbidity and mortality as well as total mortality. However, BP lowering was accepted as a primary outcome for lifestyle modification recommendations and progressive renal impairment was also accepted for patients with CKD. Randomized controlled trials (RCTs) and systematic reviews of randomized trials were selected for treatment recommendations and cross sectional and cohort studies were reviewed for assessing diagnosis and prognosis. Study characteristics and study quality were assessed using pre-specified, standardized algorithms for RCTs and cohort studies developed by CHEP.

Draft recommendations were developed for each section by national and international hypertension experts based on review of all identified articles relevant to their topic area (see Supplemental Appendix S1). Members of the Canadian Diabetes Association Guidelines Committee, Canadian Society of Nephrology, Canadian Stroke Network, and the Canadian Cardiovascular Harmonized National Guideline Endeavour Initiative also collaborated with CHEP subgroup members for the development of 2012 draft recommendations to ensure harmonized hypertension recommendations between guidelines. Cardiovascular and mortality benefits as well as adverse effects and risks were considered when formulating the draft recommendations. Costs were not considered. Subsequently, the central review committee composed of clinical epidemiologists, reviewed draft recommendations from each subgroup and, in an iterative process, helped to refine and standardize all recommendations and their grading across subgroups; recommendations were classified according to the strength of evidence (for details, see Table 1), ranging from A (strongest evidence, high-precision randomized clinical trials) to D (expert opinion alone). CHEP members then discussed and vetted the draft recommendations and evidence from each subgroup at the 2012 consensus conference held in Alliston, Ontario. Based on the deliberations at the consensus conference, the 2012 recommendations were finalized and then submitted to all 65 voting members of the CHEP Evidence-Based Recommendations Task Force for approval. External observers from the Canadian Agency for Drugs and Health, the Brazilian Society of Cardiology, and the Public Health Agency of Canada were also present at the consensus meeting. Members with conflicts of interest were recused from voting on the specific recommendations (a list of conflicts can be found in Supplemental Appendix S2). Recommendations were finalized after achieving consensus, defined as recommendations approved by > 70% of the task force. In the actual vote, all recommendations received at least 80% approval.

| Grade A | Recommendations are based on randomized trials (or systematic reviews of trials) with high levels of internal validity and statistical precision, and for which the study results can be directly applied to patients because of similar clinical characteristics and the clinical relevance of the study outcomes. |
| Grade B | Recommendations are based on randomized trials, systematic reviews or pre-specified subgroup analyses of randomized trials that have lower precision, or there is a need to extrapolate from studies because of differing populations or reporting of validated intermediate/surrogate outcomes. |
| Grade C | Recommendations from trials that have lower levels of internal validity and/or precision, or report unvalidated surrogate outcomes, or results from nonrandomized observational studies. |
| Grade D | Recommendations are based on expert opinion alone. |

The 2012 CHEP Diagnosis and Assessment Recommendations

I. Accurate measurement of BP

Recommendations

1. Health care professionals who have been specifically trained to measure BP accurately should assess BP in all adult patients at all appropriate visits to determine cardiovascular risk and monitor antihypertensive treatment (Grade D).
2. Use of standardized measurement techniques (see Supplemental Table S1) is recommended when assessing BP (Grade D).
3. Automated office BP measurements (OBPM) can be used in the assessment of office BP (Grade D).
4. When used in proper conditions, automated office systolic BP (SBP) of ≥ 135 mm Hg or diastolic BP (DBP) of ≥ 85 mm Hg should be considered analogous to mean awake ambulatory SBP of ≥ 135 mm Hg and DBP of ≥ 85 mm Hg, respectively (Grade D).

Background. Several automated OBPM devices have been independently validated for clinical accuracy, including the BpTRU automatic BP monitor, the BPM-100 electronic oscillometric office BP monitor (VSM MedTech Ltd, Vancouver, BC), and the Omron office digital BP HEM-907 monitor (Omron Healthcare Inc, Lake Forest, IL). However, further research is needed to determine whether automated OBPM accurately predict future target organ damage and cardiovascular events better than manual OBPM. CHEP is actively evaluating this area.
II. Criteria for diagnosis of hypertension and recommendations for follow-up (Fig. 1)

**Recommendations**

1. At initial presentation, patients demonstrating features of a hypertensive urgency or emergency (Table 2) should be diagnosed as hypertensive and require immediate management (Grade D).

2. If SBP is \( \geq 140 \, \text{mm Hg} \) and/or DBP is \( \geq 90 \, \text{mm Hg} \), a specific visit should be scheduled for the assessment of hypertension (Grade D). If BP is high-normal (SBP 130-139 mm Hg and/or DBP 85-89 mm Hg), annual follow-up is recommended (Grade C).

3. At the initial visit for the assessment of hypertension, if SBP is \( \geq 140 \) and/or DBP is \( \geq 90 \, \text{mm Hg} \), more than 2 additional readings should be taken during the same visit using a validated device and according to the recommended procedure for accurate BP determination (see Supplemental Table S1). The first reading should be discarded and the latter 2 readings averaged. A history and physical examination would be required (Grade C).

**Figure 1.** The expedited assessment and diagnosis of patients with hypertension: focus on validated technologies for BP assessment.

**Thresholds refer to BP values averaged across the corresponding number of visits and not just the most recent office visit. ABPM, ambulatory BP measurement; BP, blood pressure (mm Hg); DBP, diastolic BP (mm Hg); HBPM, home BP measurement; HTN, hypertension; OBPM, office BP measurement; SBP, systolic BP (mm Hg). Reprinted with permission from the Canadian Hypertension Education Program.
Table 2. Examples of hypertensive urgencies and emergencies

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic diastolic BP ≥ 130 mm Hg</td>
</tr>
<tr>
<td>Severe elevation of BP in the setting of any of:</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
</tr>
<tr>
<td>Acute aortic dissection</td>
</tr>
<tr>
<td>Acute left ventricular failure</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
</tr>
<tr>
<td>Acute kidney injury</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
</tr>
<tr>
<td>Acute ischemic stroke</td>
</tr>
<tr>
<td>Eclampsia of pregnancy</td>
</tr>
</tbody>
</table>

BP, blood pressure.

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Table 3. Examples of target organ damage

<table>
<thead>
<tr>
<th>Cerebrovascular disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Ischemic stroke and transient ischemic attack</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
</tr>
<tr>
<td>Aneurysmal subarachnoid hemorrhage</td>
</tr>
<tr>
<td>Dementia</td>
</tr>
<tr>
<td>Vascular dementia</td>
</tr>
<tr>
<td>Mixed vascular dementia and dementia of the Alzheimer’s type</td>
</tr>
<tr>
<td>Hypertensive retinopathy</td>
</tr>
<tr>
<td>Left ventricular dysfunction</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
</tr>
<tr>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Angina pectoris</td>
</tr>
<tr>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Renal disease</td>
</tr>
<tr>
<td>Chronic kidney disease (GFR &lt; 60 mL per minute per 1.73 m²)</td>
</tr>
<tr>
<td>Albuminuria</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
</tr>
<tr>
<td>Intermittent claudication</td>
</tr>
</tbody>
</table>

GFR, glomerular filtration rate.

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Table 4. Examples of key cardiovascular risk factors for atherosclerosis

<table>
<thead>
<tr>
<th>Modifiable Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 55 years</td>
</tr>
<tr>
<td>Male Family history of premature cardiovascular disease (age &lt; 55 in men and &lt; 65 in women)</td>
</tr>
</tbody>
</table>

Prior history of clinically overt atherosclerotic disease indicates a very high risk for a recurrent atherosclerotic event (eg, peripheral arterial disease, previous stroke, or transient ischemic attack).

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Table 5. Examples of exogenous factors that can induce/aggravate hypertension

<table>
<thead>
<tr>
<th>Exogenous Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription drugs</td>
</tr>
<tr>
<td>NSAIDs, including coxibs</td>
</tr>
<tr>
<td>Corticosteroids and anabolic steroids</td>
</tr>
<tr>
<td>Oral contraceptive and sex hormones</td>
</tr>
<tr>
<td>Vasoconstricting/sympathomimetic decongestants</td>
</tr>
<tr>
<td>Calcineurin inhibitors (cyclosporin, tacrolimus)</td>
</tr>
<tr>
<td>Erythropoietin and analogues</td>
</tr>
<tr>
<td>Antidepressants: MAOIs, SNRIs, SSRIs</td>
</tr>
<tr>
<td>Mildodrine</td>
</tr>
<tr>
<td>Other substances</td>
</tr>
<tr>
<td>Lorcice root</td>
</tr>
<tr>
<td>Stimulants including cocaine</td>
</tr>
</tbody>
</table>

MAOIs, monoamine oxidase inhibitors; NSAIDs, nonsteroidal anti-inflammatory drugs; SNRIs, serotonin-norepinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors.

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7. If at the last diagnostic visit the patient is not diagnosed as hypertensive and has no evidence of macrovascular target organ damage, the patient’s BP should be assessed at yearly intervals (Grade D).

8. Hypertensive patients receiving lifestyle modification advice alone (nonpharmacological treatment) should be followed up at 3- to 6-month intervals. Shorter intervals (every 1 or 2 months) are needed for patients with higher BP (Grade D).

9. Patients given antihypertensive drug treatment should be seen monthly or every 2 months, depending on the level of BP, until readings on 2 consecutive visits are below their target (Grade D). Shorter intervals between visits will be needed for symptomatic patients and those with severe hypertension, intolerance to antihypertensive drugs, or target organ damage (grade D). When the target BP has been reached, patients should be seen at 3- to 6-month intervals (grade D).

**Background.** White coat hypertension is associated with a better cardiovascular prognosis compared with those with elevated BP at the office and in nonoffice settings. However, diagnosing white coat hypertension is challenging and has relied on 24-hour ABPM to confirm its diagnosis. There is now cumulative evidence to indicate that repeated HBPM provides significant prognostic accuracy to be used in confirming white coat hypertension. Recent evidence from 163 subjects enrolled in an observational study suggests that HBPM demonstrated the lowest variability when compared with office and ambulatory monitoring. Within-person variability improved with longer self-monitoring duration and lower intervals between monitoring; the lowest coefficients of variation (2.7%) was achieved after 4 weeks of monitoring without intervals, and the highest (6.1%) when there was a 10-week interval in a total of 1 week duration of measurements. Although it is recognized that neither HBPM nor ABPM are perfectly reproducible and have moderate diagnostic agreement, patients with white coat hypertension diagnosed by either HBPM or awake-ABPM were shown to have a more favourable risk profile and less target organ damage than those with sustained hypertension, with the percentage of patients with high or very high cardiovascular risk decreasing progressively from sustained hypertension to white coat hypertension confirmed by both techniques (P < 0.005 for trend). Furthermore, longitudinal evidence suggests that HBPM has a better prognostic accuracy than OBPM; the incidence of cardiovascular events in patients with white coat syndrome was high and not significantly different from the incidence of cardiovascular events in patients with controlled hypertension (hazard ratio [HR], 1.18, 95% confidence interval [CI], 0.67-2.10).

**III. Assessment of overall cardiovascular risk in hypertensive patients**

**Recommendations**

1. Global cardiovascular risk should be assessed. Multifactorial risk assessment models can be used to predict more accurately an individual’s global cardiovascular risk (Grade A) and to use antihypertensive therapy more efficiently (Grade D). In the absence of Canadian data to determine the accuracy of risk calculations, avoid using absolute levels of risk to support treatment decisions (Grade C).

2. Consider informing patients of their global risk to improve the effectiveness of risk factor modification (Grade B). Consider also using analogies that describe comparative risk such as “cardiovascular age,” “vascular age,” or “heart age” to inform patients of their risk status (Grade B).

**Background.** Risk calculators are freely available at: www.myhealthcheckup.com, and www.monbilansante.com. The Systematic Cerebrovascular and Coronary Risk Evaluation (SCORE) risk calculation was updated using Canadian data and is now available at http://www.scorecanada.ca. There are no changes to these recommendations for 2012.

**IV. Routine and optional laboratory tests for the investigation of patients with hypertension**

**Recommendations**

1. Routine laboratory tests that should be performed for the investigation of all patients with hypertension include the following:
   i. Urinalysis (Grade D);
   ii. Blood chemistry (potassium, sodium, and creatinine) (Grade D);
   iii. Fasting blood glucose (Grade D);
   iv. Fasting serum total cholesterol and high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides (Grade D);
   v. Standard 12-lead electrocardiography (Grade C).

2. Assess urinary albumin excretion in patients with diabetes (Grade D).

3. All treated hypertensive patients should be monitored according to the current Canadian Diabetes Association guidelines for the new appearance of diabetes (Grade B).

4. During the maintenance phase of hypertension management, tests (including those for electrolytes, creatinine, and fasting lipids) should be repeated with a frequency reflecting the clinical situation (Grade D).

**Background.** There are no changes to these recommendations for 2012.

**V. Assessment for renovascular hypertension**

**Recommendations**

1. Patients presenting with ≥ 2 of the clinical clues listed next, suggesting renovascular hypertension, should be investigated (Grade D):
   i. Sudden onset or worsening of hypertension and age > 55 or < 30 years;
   ii. Presence of an abdominal bruit;
   iii. Hypertension resistant to ≥ 3 drugs;
   iv. Rise in serum creatinine level ≥ 30% associated with use of an angiotensin-converting enzyme (ACE) inhibitor or ARB;
   v. Other atherosclerotic vascular disease, particularly in patients who smoke or have dyslipidemia;
   vi. Recurrent pulmonary edema associated with hypertensive surges. When available, the following tests are recommended to aid in the usual screening for renal vascular disease: captopril-enhanced radioisotope renal scan, Doppler sonography, magnetic resonance angiography, and computed tomography angiography (for those with normal renal function) (Grade B). Captopril-enhanced radio-
Background. There are no changes to these recommendations for 2012.

VI. Endocrine hypertension

Recommendations

A. Hyperaldosteronism: screening and diagnosis

1. Screening for hyperaldosteronism should be considered for the following patients (Grade D):
   i. Hypertensive patients with spontaneous hypokalemia ($K^+ < 3.5$ mmol/L);
   ii. Hypertensive patients with marked diuretic-induced hypokalemia ($K^+ < 3.0$ mmol/L);
   iii. Patients with hypertension refractory to treatment with $\geq 3$ drugs;
   iv. Hypertensive patients found to have an incidental adrenal adenoma.

2. Screening for hyperaldosteronism should include assessment of plasma aldosterone and plasma renin activity (Supplemental Table S2).

3. For patients with suspected hyperaldosteronism (on the basis of the screening test, Supplemental Table S2, Item 3), a diagnosis of primary aldosteronism should be established by demonstrating inappropriate autonomous hypersecretion of aldosterone using at least one of the manoeuvres listed in Supplemental Table S2, Item 4. When the diagnosis is established, the abnormality should be localized using any of the tests described in Supplemental Table S2, Item 5.

B. Pheochromocytoma: screening and diagnosis

1. If pheochromocytoma is strongly suspected, the patient should be referred to a specialized hypertension centre, particularly if biochemical screening tests (Supplemental Table S3) have already been found to be positive (Grade D).

2. The following patients should be considered for screening for pheochromocytoma (Grade D):
   i. Patients with paroxysmal and/or severe (BP $\geq 180/110$ mm Hg) sustained hypertension refractory to usual antihypertensive therapy;
   ii. Patients with hypertension and multiple symptoms suggestive of catecholamine excess (eg, headaches, palpitations, sweating, panic attacks, and pallor);
   iii. Patients with hypertension triggered by $\beta$-blockers, monoamine oxidase inhibitors, micturition, or changes in abdominal pressure;
   iv. Patients with incidentally discovered adrenal mass and patients with hypertension and multiple endocrine neoplasia 2A or 2B, von Recklinghausen’s neurofibromatosis, or von Hippel-Lindau disease;
   v. For patients with positive biochemical screening tests, localization of pheochromocytomas should involve the use of magnetic resonance imaging (preferable), computed tomography (if magnetic resonance imaging unavailable), and/or iodine I-131 meta-iodobenzylguanidine scintigraphy (Grade C for each modality).

Background. There are no changes to these recommendations for 2012.

VII. HBPM

Recommendations

1. HBPM can be used in the diagnosis of hypertension (Grade C).

2. The use of HBPM on a regular basis should be considered for patients with hypertension, particularly those with:
   i. Diabetes mellitus (Grade D);
   ii. CKD (Grade C);
   iii. Suspected nonadherence (Grade D);
   iv. Demonstrated white coat effect (Grade C);
   v. BP controlled in the office but not at home (masked hypertension) (Grade C).

3. When white coat hypertension is suggested by HBPM, its presence should be confirmed by repeat HBPM (see Recommendation 8) or ABPM before treatment decisions are made (Grade D).

4. Patients should be advised to purchase and use only HBPM devices that are appropriate for the individual and have met standards of the Association for the Advancement of Medical Instrumentation, the most recent requirements of the British Hypertension Society protocol, or the International Protocol for validation of automated BP measuring devices. Patients should be encouraged to use devices with data recording capabilities or automatic data transmission to increase the reliability of reported HBPM (Grade D).

5. Home SBP values $\geq 135$ mm Hg or DBP values $\geq 85$ mm Hg should be considered elevated and associated with an increased overall mortality risk analogous to office SBP readings of $\geq 140$ mm Hg or DBP $\geq 90$ mm Hg (Grade C).

6. Health care professionals should ensure that patients who measure their BP at home have adequate training and, if necessary, repeat training in measuring their BP. Patients should be observed to determine that they measure BP correctly and should be given adequate information about interpreting these readings (Grade D).

7. The accuracy of all individual patients’ validated devices (including electronic devices) must be regularly checked against a device of known calibration (Grade D).

8. HBPM for assessing white coat hypertension or sustained hypertension should be based on duplicate measures, morning and evening, for an initial 7-day period. First-day home BP values should not be considered (Grade D).


Updated background information on white coat hypertension is provided in section II. Criteria for Diagnosis of Hypertension and Recommendations for Follow-up. There are no other changes to these recommendations for 2012.

VIII. ABPM

Recommendations

1. BP monitoring can be used in the diagnosis of hypertension (Grade C). ABPM should be considered when an office-induced increase in BP is suspected in treated patients with:
i. BP that is not below target despite receiving appropriate chronic antihypertensive therapy (Grade C);
ii. Symptoms suggestive of hypotension (Grade C);
iii. Fluctuating office BP readings (Grade D).
2. Physicians should use only ABPM devices that have been validated independently using established protocols (Grade D).
3. Therapy adjustment should be considered in patients with a mean 24-hour ambulatory SBP of ≥ 130 mm Hg or DBP of ≥ 80 mm Hg or a mean awake SBP of ≥ 135 mm Hg or DBP of ≥ 85 mm Hg (Grade D).
4. The magnitude of changes in nocturnal BP should be taken into account in any decision to prescribe or withhold drug therapy based upon ABPM (Grade C) because a decrease in nocturnal BP of < 10% is associated with increased risk of cardiovascular events.

Background. There are no changes to these recommendations for 2012.

IX. Role of echocardiography

Recommendations

1. Routine echocardiographic evaluation of all hypertensive patients is not recommended (Grade D).
2. An echocardiogram for assessment of left ventricular hypertrophy is useful in selected cases to help define the future risk of cardiovascular events (Grade C).
3. Echocardiographic assessment of left ventricular mass, as well as of systolic and diastolic left ventricular function is recommended for hypertensive patients suspected to have left ventricular dysfunction or coronary artery disease (Grade D).
4. Patients with hypertension and evidence of heart failure should have an objective assessment of left ventricular EF, either by echocardiogram or nuclear imaging (Grade D).

Background. There are no changes to these recommendations for 2012.

The CHEP 2012 Prevention and Treatment Recommendations

I. Lifestyle management

Recommendations

A. Physical exercise

1. For nonhypertensive individuals (to reduce the possibility of becoming hypertensive) or for hypertensive patients (to reduce their BP), prescribe the accumulation of 30-60 minutes of moderate intensity dynamic exercise (eg, walking, jogging, cycling or swimming) 4-7 days per week in addition to the routine activities of daily living (Grade D). Higher intensities of exercise are not more effective (Grade D).

B. Weight reduction

1. Height, weight, and waist circumference should be measured, and body mass index calculated for all adults (Grade D).
2. Maintenance of a healthy body weight (body mass index 18.5 to 24.9, and waist circumference < 102 cm for men and < 88 cm for women) is recommended for nonhypertensive individuals to prevent hypertension (Grade C) and for hypertensive patients to reduce BP (Grade B). All overweight hypertensive individuals should be advised to lose weight (Grade B).
3. Weight loss strategies should employ a multidisciplinary approach that includes dietary education, increased physical activity, and behavioural intervention (Grade B).

C. Alcohol consumption

1. To reduce BP, alcohol consumption should be in accordance with Canadian low-risk drinking guidelines in both normotensive and hypertensive individuals. Healthy adults should limit alcohol consumption to ≤ 2 drinks per day, and consumption should not exceed 14 standard drinks per week for men and 9 standard drinks per week for women (Grade B). (Note: One standard drink is considered to be equivalent of 13.6 g or 17.2 mL of ethanol or approximately 44 mL [1.5 oz] of 80 proof [40%] spirits, 355 mL [12 oz] of 5% beer, or 148 mL [5 oz] of 12% wine).

D. Dietary recommendations

1. It is recommended that hypertensive patients and normotensive individuals at increased risk of developing hypertension consume a diet that emphasizes fruits, vegetables, low-fat dairy products, dietary and soluble fibre, whole grains, and protein from plant sources that is reduced in saturated fat and cholesterol (Dietary Approaches to Stop Hypertension [DASH] diet41-44) (Supplemental Table S4) (Grade B).

E. Sodium intake

1. For prevention and treatment of hypertension, a dietary sodium intake of 1500 mg (65 mmol) per day is recommended for adults aged ≤ 50 years; 1300 mg (57 mmol) per day for age 51-70 years; and 1200 mg (52 mmol) per day for age > 70 years (Grade B).

F. Potassium, calcium, and magnesium intake

1. Supplementation of potassium, calcium, and magnesium is not recommended for the prevention or treatment of hypertension (Grade B).

G. Stress management

1. In hypertensive patients in whom stress may be contributing to BP elevation, stress management should be considered as an intervention (Grade D). Individualized cognitive-behavioural interventions are more likely to be effective when relaxation techniques are used (Grade B).

Background. There are no changes to these recommendations for 2012.

II. Indications for drug therapy for adults with hypertension without compelling indications for specific agents

Recommendations

1. Antihypertensive therapy should be prescribed for average DBP measurements of ≥ 100 mm Hg (Grade A) or average SBP measurements of ≥ 160 mm Hg (Grade A) in patients without macrovascular target organ damage or other cardiovascular risk factors.
2. Antihypertensive therapy should be strongly considered if DBP readings average ≥ 90 mm Hg in the presence of...
macrovacular target organ damage or other independent cardiovascular risk factors (Grade A).

3. Antihypertensive therapy should be strongly considered if SBP readings average ≥ 140 mm Hg in the presence of macrovacular target organ damage (Grade C for 140-160 mm Hg; Grade A for > 160 mm Hg).

4. Antihypertensive therapy should be considered in all patients meeting the above indications regardless of age (Grade B). Caution should be exercised in elderly patients who are frail.

Background. There are no changes to these recommendations for 2012.

III. Choice of therapy for adults with hypertension without compelling indications for specific agents

Recommendations

A. Recommendations for individuals with diastolic and/or systolic hypertension

1. Initial therapy should be monotherapy with a thiazide diuretic (Grade A), a β-blocker (in patients younger than 60 years, Grade B), an ACE inhibitor (in nonblack patients, Grade B), a long-acting calcium channel blocker (CCB) (Grade B); or an ARB (Grade B). If there are adverse effects, another drug from this group should be substituted. Hypokalemia should be avoided in patients treated with thiazide diuretic monotherapy (Grade C).

2. Additional antihypertensive drugs should be used if target BP levels are not achieved with standard-dose monotherapy (Grade B). Add-on drugs should be chosen from first-line choices. Useful choices include a thiazide diuretic or CCB with either: ACE inhibitor, ARB, or β-blocker (Grade B for the combination of thiazide diuretic and a dihydropyridine CCB; Grade C for the combination of dihydropyridine CCB and ACE inhibitor; and Grade D for all other combinations). Caution should be exercised in combining a nondihydropyridine CCB and a β-blocker (Grade D). The combination of an ACE inhibitor and an ARB is not recommended (Grade A).

3. Combination therapy using 2 first-line agents may also be considered as initial treatment of hypertension (Grade C) if SBP is 20 mm Hg above target or if DBP is 10 mm Hg above target. However, caution should be exercised in patients in whom a substantial fall in BP from initial combination therapy is more likely to occur or in whom it would be poorly tolerated (eg, elderly patients).

4. If BP is still not controlled with a combination of 2 or more first-line agents, or there are adverse effects, other antihypertensive drugs may be added (Grade D).

5. Possible reasons for poor response to therapy (Table 6) should be considered (Grade D).

6. α-Blockers are not recommended as first-line agents for uncomplicated hypertension (Grade A); β-blockers are not recommended as first-line therapy for uncomplicated hypertension in patients 60 years of age or older (Grade A); and ACE inhibitors are not recommended as first-line therapy for uncomplicated hypertension in black patients (Grade A). However, these agents may be used in patients with certain comorbid conditions or in combination therapy.

Table 6. Possible reasons for poor response to antihypertensive therapy

<table>
<thead>
<tr>
<th>Reason</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noncompliance</td>
<td>Dietary</td>
</tr>
<tr>
<td>Dietary</td>
<td>Medication</td>
</tr>
<tr>
<td>Associated conditions</td>
<td>Obesitvity</td>
</tr>
<tr>
<td>Obesity</td>
<td>Cigarette smoking</td>
</tr>
<tr>
<td>Excessive alcohol consumption</td>
<td>Sleep apnea</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>Drug interactions</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td></td>
</tr>
<tr>
<td>(including cyclo-oxygenase-2 inhibitors)</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>Corticosteroids and anabolic steroids</td>
</tr>
<tr>
<td>Sympathomimetics and decongestants</td>
<td>Cocaine</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Erythropoietin</td>
</tr>
<tr>
<td>Cyclosporine, tacrolimus</td>
<td>Lecitcne</td>
</tr>
<tr>
<td>Over-the-counter dietary supplements</td>
<td></td>
</tr>
<tr>
<td>(eg, ephedra, ma huang, bitter orange)</td>
<td></td>
</tr>
<tr>
<td>Monoamine oxidase inhibitors, certain</td>
<td></td>
</tr>
<tr>
<td>selective serotonin reuptake inhibitors</td>
<td></td>
</tr>
<tr>
<td>and serotonin-norepinephrine reuptake inhibitors</td>
<td></td>
</tr>
<tr>
<td>Suboptimal treatment regimens</td>
<td></td>
</tr>
<tr>
<td>Dosage too low</td>
<td></td>
</tr>
<tr>
<td>Inappropriate combinations of antihypertensive agents</td>
<td></td>
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<tr>
<td>Volume overload</td>
<td></td>
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<tr>
<td>Excessive salt intake</td>
<td></td>
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<tr>
<td>Renal sodium retention (pseudotolerance)</td>
<td></td>
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<tr>
<td>Secondary hypertension</td>
<td></td>
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<tr>
<td>Renal insufficiency</td>
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<tr>
<td>Renovascular disease</td>
<td></td>
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<tr>
<td>Primary hyperaldosteronism</td>
<td></td>
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<tr>
<td>Thyroid disease</td>
<td></td>
</tr>
<tr>
<td>Phaeochromocytoma and other rare endocrine causes</td>
<td></td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td></td>
</tr>
</tbody>
</table>

Note that causes of ‘pseudo-resistance’ (such as white coat hypertension or pseudo-hypertension in the elderly) should be ruled out first. Adapted from McAlister et al.46

B. Recommendations for individuals with isolated systolic hypertension

1. Initial therapy should be monotherapy with a thiazide diuretic (Grade A), a long-acting dihydropyridine CCB (Grade A), or an ARB (Grade B). If there are adverse effects, another drug from this group should be substituted. Hypokalemia should be avoided in patients treated with thiazide diuretic monotherapy (Grade C).

2. Additional antihypertensive drugs should be used if target BP levels are not achieved with standard-dose monotherapy (Grade B). Add-on drugs should be chosen from first-line options (Grade D).

3. If BP is still not controlled with a combination of 2 or more first-line agents, or there are adverse effects, other classes of drugs (such as α-blockers, ACE inhibitors, centrally acting agents or nondihydropyridine CCBs) may be added or substituted (Grade D).

4. Possible reasons for poor response to therapy (Table 6) should be considered (Grade D).

5. α-Blockers are not recommended as first-line agents for uncomplicated isolated systolic hypertension (Grade A); and β-blockers are not recommended as first-line therapy for isolated systolic hypertension in patients aged ≥ 60 years.
Table 7. Cardiovascular risk factors for consideration of statin therapy in nondyslipidemic patients with hypertension

<table>
<thead>
<tr>
<th>Male sex</th>
<th>Age ≥ 55 years</th>
<th>Left ventricular hypertrophy</th>
<th>Other electrocardiogram abnormalities: left bundle branch block, left ventricular strain pattern, abnormal QT-waves or ST-T changes compatible with ischemic heart disease</th>
<th>Peripheral arterial disease</th>
<th>Previous stroke or transient ischemic attack</th>
<th>Microalbuminuria or proteinuria</th>
<th>Diabetes mellitus</th>
<th>Smoking</th>
<th>Family history of premature cardiovascular disease</th>
<th>Total cholesterol to high-density lipoprotein ratio 6</th>
</tr>
</thead>
</table>

If hypertensive patients have ≥ 3 of these risk factors, statins should be considered.

Data from Sever et al.47

(Grade A). However, both agents may be used in patients with certain comorbid conditions or in combination therapy.

Background. Recent concern was raised regarding the potential association of cancer with ARBs amid publication of several recent post hoc analyses. The 2012 guidelines continue to recommend the use of ARBs in appropriate clinical situations given the completed safety analysis commissioned by the US Food and Drug Administration of 31 clinical trials and 156,000 patients finding no evidence of an increased risk of cancer in patients who take an ARB.46 There are no changes to these recommendations.

IV. Global vascular protection therapy for adults with hypertension without compelling indications for specific agents

Recommendations

1. Statin therapy is recommended in hypertensive patients with 3 or more cardiovascular risk factors as defined in Table 7 (Grade A in patients > 40 years), or with established atherosclerotic disease (Grade A regardless of age).

2. Strong consideration should be given to the addition of low-dose acetylsalicylic acid therapy in hypertensive patients (Grade A in patients > 50 years). Caution should be exercised if BP is not controlled (Grade C).

Background. There are no changes to these recommendations for 2012. For further guidance in the management of patients with dyslipidemia, readers are referred to the 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult.48

V. Goal of therapy for adults with hypertension without compelling indications for specific agents

Recommendations

1. The SBP treatment goal is a pressure level of < 140 mm Hg (Grade C). The DBP treatment goal is a pressure level of < 90 mm Hg (Grade A).

Background. There are no changes to these recommendations for 2012.

VI. Treatment of hypertension in association with ischemic heart disease

Recommendations

A. Recommendations for hypertensive patients with coronary artery disease

1. An ACE inhibitor or ARB is recommended for most patients with hypertension and coronary artery disease (Grade A).

2. For patients with stable angina, β-blockers are preferred as initial therapy (Grade B). CCBs may also be used (Grade B).

3. Short-acting nifedipine should not be used (Grade D).

4. For patients with coronary artery disease, but without co-existing systolic heart failure, the combination of an ACE inhibitor and ARB is not recommended (Grade B).

5. In high-risk patients, when combination therapy is being used, choices should be individualized. The combination of an ACE inhibitor and a dihydropriridine CCB is preferable to an ACE inhibitor and a diuretic in selected patients (Grade A).

B. Recommendations for patients with hypertension who have had a recent myocardial infarction

1. Initial therapy should include both a β-blocker and an ACE inhibitor (Grade A).

2. An ARB can be used if the patient is intolerant of an ACE inhibitor (Grade A in patients with left ventricular systolic dysfunction).

3. CCBs may be used in postmyocardial infarction patients when β-blockers are contraindicated or not effective. Non-dihydropyridine CCBs should not be used when there is heart failure, as evidenced by pulmonary congestion on examination or radiography (Grade D).

Background. There are no changes to these recommendations for 2012.

VII. Treatment of hypertension in association with heart failure

Recommendations

1. In patients with systolic dysfunction (ejection fraction \(\text{EF}<40\%\)), ACE inhibitors (Grade A) and β-blockers (Grade A) are recommended for initial therapy. Aldosterone antagonists (mineralocorticoid receptor antagonists) may be added for patients with a recent cardiovascular hospitalization, acute myocardial infarction, elevated B-type natriuretic peptide or NT-proBNP. Other diuretics may be added as additional therapy if needed (Grade B for thiazide diuretics for BP control, Grade D for loop diuretics for volume control). Beyond considerations of BP control, doses of ACE inhibitors or ARBs should be titrated to those found to be effective in trials unless adverse effects become manifest (Grade B).

2. An ARB is recommended if ACE inhibitors are not tolerated (Grade A).

3. A combination of hydralazine and isosorbide dinitrate is recommended if ACE inhibitors and ARBs are contraindicated or not tolerated (Grade B).
4. For hypertensive patients whose BP is not controlled, an ARB may be added to an ACE inhibitor and other antihypertensive drug treatment (Grade A). Careful monitoring should be used if combining an ACE inhibitor and an ARB due to potential adverse effects such as hypotension, hyperkalemia, and worsening renal function (Grade C). Additional therapies may also include dihydropyridine CCBs (Grade C).

**Background.** This year, we have expanded our recommendations for mineralocorticoid receptor antagonists in patients with both hypertension and chronic systolic heart failure (EF < 40%) on the basis of compelling evidence from 3 RCTs. Our previous recommendation was guided by 2 earlier trials, RALES and EPHESUS. This year, the EMPHASIS-HF provided definite evidence that establishes the beneficial effect of mineralocorticoid receptor antagonists on morbidity and mortality across a broad spectrum of systolic heart failure patients. EMPHASIS-HF enrolled 2737 patients with heart failure, who were randomized to receive either the mineralocorticoid receptor antagonist eplerenone (up to 50 mg daily) or placebo in addition to recommended therapy. Patients were included if they were at least 55 years of age, had NYHA functional class II symptoms, an EF of no more than 30% (or, if > 30% to 35%, a QRS duration > 130 ms on electrocardiogram) and treatment with an ACE inhibitor, an ARB or both, and a β-blocker (unless contraindicated) at the recommended dose or maximal tolerated dose. The trial was stopped prematurely after a median follow-up period of 21 months. The primary outcome, a composite of death from cardiovascular causes or hospitalization for heart failure, was significantly reduced in the eplerenone group when compared with the placebo group (HR, 0.63; 95% CI, 0.54-0.74) as was risk of death (HR, 0.76; 95% CI, 0.62-0.93). Importantly, excluded from the trial were patients with a baseline serum potassium level > 5.0 mmol/L and a baseline estimated GFR < 30 mL per minute per 1.73m². Despite this, compared with placebo there was a more than 2-fold increased risk of hyperkalemia in the eplerenone group (3.7% vs 8.0%, respectively, P < 0.001). This finding, coupled with earlier concerns regarding the risk of hyperkalemia with spironolactone in more severe stages of heart failure, and in combination with other renin angiotensin antagonists underscores the importance of regular electrolyte monitoring in patients who receive mineralocorticoid receptor antagonists. Thus, most patients with CKD and those with a history of severe hyperkalemia should not receive a mineralocorticoid receptor antagonist.

This year, data from 3 ARB RCTs including patients with hypertension and AF (ACTIVE I, ANTIPAF, and GISSI-AF) were examined in detail. In ACTIVE I, irbesartan did not reduce either coprimary endpoint comprising major cardiovascular events in patients with AF and at least 1 additional stroke risk factor (HR, 0.99; 95% CI, 0.91-1.08; and HR, 0.94; 95% CI, 0.87-1.02). Although irbesartan reduced the risk of hospitalization for heart failure (HR, 0.86; 95% CI, 0.76-0.98), it did not significantly reduce the risk of hospitalization for AF (HR, 0.95; 95% CI, 0.85-1.07). Furthermore, symptomatic hypotension was more common in the irbesartan group (P < 0.001) as was any renal dysfunction leading to drug discontinuation (P = 0.02). A similar lack of benefit for olmesartan was noted in the ANTIPAF trial (in patients with paroxysmal AF without structural heart disease in sinus rhythm at recruitment) and for valsartan in the GISSI-AF trial (in patients with a history of recurrent AF in sinus rhythm at recruitment). Based on this evidence, the Task Force concluded that ARBs did not prevent recurrent AF or major cardiovascular events in patients with AF. Therefore, the presence of AF in patients with hypertension should not mandate selection of an ARB for the treatment of hypertension.

**VIII. Treatment of hypertension in association with stroke**

**Recommendations**

A. BP management in acute stroke (onset to 72 hours)

1. For patients with ischemic stroke not eligible for thrombolytic therapy, treatment of hypertension in the setting of acute ischemic stroke or transient ischemic attack should not be routinely undertaken (Grade D). Extreme BP elevation (eg, SBP > 220 mm Hg or DBP > 120 mm Hg) may be treated to reduce the BP by approximately 15% (Grade D), and not more than 25%, over the first 24 hours with gradual reduction thereafter (Grade D). Avoid excessive lowering of BP as this may exacerbate existing ischemia or may induce ischemia, particularly in the setting of intracranial arterial occlusion or extracranial carotid or vertebral artery occlusion (Grade D). Pharmacological agents and routes of administration should be chosen to avoid precipitous falls in BP (Grade D).

2. For patients with ischemic stroke eligible for thrombolytic therapy, very high BP (> 185/110 mm Hg) should be treated concurrently in patients receiving thrombolytic therapy for acute ischemic stroke to reduce the risk of secondary intracranial hemorrhage (Grade B).

B. BP management after acute stroke

1. Strong consideration should be given to the initiation of antihypertensive therapy after the acute phase of a stroke or transient ischemic attack (Grade A).

2. After the acute phase of a stroke, BP-lowering treatment is recommended to a target of consistently < 140/90 mm Hg (Grade C).

3. Treatment with an ACE inhibitor/diuretic combination is preferred (Grade B).

4. For patients with stroke, the combination of an ACE inhibitor and ARB is not recommended (Grade B).

**Background.** There are no changes to these recommendations for 2012.

**IX. Treatment of hypertension in association with left ventricular hypertrophy**

**Recommendations**

1. Hypertensive patients with left ventricular hypertrophy should be treated with antihypertensive therapy to lower the rate of subsequent cardiovascular events (Grade C).

2. The choice of initial therapy can be influenced by the presence of left ventricular hypertrophy (Grade D). Initial therapy can be drug treatment using ACE inhibitors, ARBs, long-acting CCBs, or thiazide diuretics. Direct arterial vasodilators such as hydralazine or minoxidil should not be used.
Background. There are no changes to these recommendations for 2012.

X. Treatment of hypertension in association with nondiabetic CKD

Recommendations

1. For patients with nondiabetic CKD, target BP is < 140/90 mm Hg (Grade B).
2. For patients with hypertension and proteinuric CKD (urinary protein > 500 mg/24 hours or albumin-to-creatinine ratio > 30 mg/mmol), initial therapy should be an ACE inhibitor (Grade A) or an ARB if there is intolerance to ACE inhibitors (Grade B).
3. Thiazide diuretics are recommended as additive antihypertensive therapy (Grade D). For patients with CKD and volume overload, loop diuretics are an alternative (Grade D).
4. In most cases, combination therapy with other antihypertensive agents may be needed to reach target BP levels (Grade D).
5. The combination of an ACE inhibitor and ARB is not recommended for patients with nonproteinuric CKD (Grade B).

Background. This year, the results of 3 RCTs were examined in detail and led to the revision of the previous BP target for hypertensive patients with nondiabetic CKD.

The MDRD trial included patients with GFR between 13 and 55 mL per minute per 1.73m² who were randomly assigned to either a usual BP target (mean arterial pressure [MAP], 107 mm Hg, equivalent to 140/90 mm Hg) or a low BP target (MAP 92 mm Hg, equivalent to 125/75 mm Hg). In the primary analysis, there was no difference between the usual and low BP groups with respect to the slope of decline in GFR. Secondary outcomes including kidney failure, death, a composite of kidney failure or death, and cardiovascular events were also not significantly different between groups. A post hoc, subgroup analysis showed that the rate of GFR decline appeared to increase above a MAP of 98 mm Hg in patients with proteinuria between 0.25-3.0 gr/day, while in patients with proteinuria of ≥ 3.0 gr/day, the rate of GFR decline increased above a MAP of 92 mm Hg. However, this post hoc analysis was limited by the fact that there was no stratification based on prespecified levels of proteinuria, a priori power calculations were not performed for subgroups, baseline patient characteristics were not presented according to subgroups, and adjustment for multiple testing was not performed. Furthermore, the use of ACE inhibitors was higher in the low BP target group.

In the AASK trial, African-American individuals with hypertensive CKD and GFR between 20 and 65 mL per minute per 1.73m² were randomly assigned to either a usual BP target (MAP, 102-107 mm Hg) or a low BP target (MAP, 92 mm Hg). In addition, patients were randomly assigned to treatment with ramipril, metoprolol, or amlodipine in a 2 × 3 factorial design. There was no significant difference in the chronic slope or the overall rate of decline in GFR per year between groups. Patients in the low BP group experienced a 17% reduction in proteinuria as compared with an increase of 7% in the usual BP group. There was no difference in the risk of other secondary outcomes including kidney failure, the composite of kidney failure or death, the component of a GFR event or death, or the combined endpoint of GFR event, kidney failure, or death. There was no difference in cardiovascular mortality or nonfatal cardiovascular events. In the original AASK trial there was an interaction between baseline proteinuria and BP target, which was not reported in the original analysis but in a subsequent analysis. Similar to the MDRD trial, this was a post hoc subgroup analysis and randomization was not stratified based on prespecified levels of proteinuria, there were no a priori power calculations for the subgroups, and adjustment for multiple testing was not performed. The suggestion that patients with proteinuria of > 300 mg/24 hours may have derived benefit from a lower BP target, and that those with less proteinuria may have derived worse outcomes, should be interpreted as hypothesis-generating.

The REIN-2 trial randomly assigned patients with nondiabetic CKD and > 1 gr/day of proteinuria to usual BP target (target DBP < 90 mm Hg) or low BP target (target BP < 130/80 mm Hg). All patients were treated with ramipril and the low BP group received felodipine 5-10 mg/day together with additional agents as needed to achieve targets. The trial was stopped early due to futility after a median follow-up of 19 months; this was defined a priori. Mean achieved BP was 134/82 mm Hg in the usual BP group compared with 130/80 mm Hg in the low BP group. There was no difference in the risk of progression to kidney failure between groups (adjusted HR, 1.0; 95% CI, 0.61-1.64). Significant limitations of this study included use of dihydropyridine CCB in the low BP group, the small difference in achieved BP (4/2 mm Hg) between groups, limited follow-up, as well as the fact that all patients received therapy with a fixed dose of an ACE inhibitor.

Overall, there is no compelling evidence to support a low BP target of < 130/80 mm Hg in all patients with hypertension and nondiabetic CKD. Despite observational evidence suggesting that more intensive BP control may be beneficial in individuals with > 300 mg/24 hours or > 1 gr/day of proteinuria, the only RCT examining this issue was negative. Although a smaller benefit cannot be ruled out, the current evidence base does not support a more intensive BP target in this group. Therefore, the Task Force voted to remove the previous low BP target and resume the general BP target (< 140/90 mm Hg) recommended for patients with hypertension.

XI. Treatment of hypertension in association with renovascular disease

Recommendations

1. Renovascular hypertension should be treated in the same manner as hypertension without compelling indications, except for caution in the use of ACE inhibitors or ARBs due to the risk of acute renal failure in bilateral disease or unilateral disease with a solitary kidney (Grade D).
2. Close follow-up and early intervention (angioplasty and stenting or surgery) should be considered for patients with uncontrolled hypertension despite therapy with ≥ 3 drugs, deteriorating kidney function, bilateral atherosclerotic renal artery lesions (or tight atherosclerotic stenosis in a single kidney), or recurrent episodes of flash pulmonary edema (Grade D).
Background. There are no changes to these recommendations for 2012.

XII. Treatment of hypertension in association with diabetes mellitus

Recommendations
1. Persons with diabetes mellitus should be treated to attain SBP of <130 mm Hg (Grade C) and DBP of <80 mm Hg (Grade A). (These target BP levels are the same as the BP treatment thresholds.) Combination therapy using 2 first-line agents may also be considered as initial treatment of hypertension (Grade B) if SBP is 20 mm Hg above target or if DBP is 10 mm Hg above target. However, caution should be exercised in patients in whom a substantial fall in BP is more likely or poorly tolerated (eg, elderly patients and patients with autonomic neuropathy).

2. For persons with cardiovascular or kidney disease, including microalbuminuria or with cardiovascular risk factors in addition to diabetes and hypertension, an ACE inhibitor or an ARB is recommended as initial therapy (Grade A).

3. For persons with diabetes and hypertension not included in the above recommendation, appropriate choices include (in alphabetical order): ACE inhibitors (Grade A), ARBs (Grade B), dihydropyridine CCBs (Grade A), and thiazide/thiazide-like diuretics (Grade A).

4. If target BP levels are not achieved with standard-dose monotherapy, additional antihypertensive therapy should be used. For persons in whom combination therapy with an ACE inhibitor is being considered, a dihydropyridine CCB is preferable to hydrochlorothiazide (Grade A).

Background. This year, 2 meta-analyses that addressed the questions about relative benefits and risks of achieving lower SBP in patients with diabetes mellitus and hypertension were published.

The Bangalore et al. meta-analysis included trials that compared achieved SBP levels of <135 mm Hg, <130 mm Hg, and <140 mm Hg in patients with diabetes or impaired fasting glucose (IFG). The primary outcome was major adverse cardiovascular events including mortality, cardiovascular mortality, myocardial infarction, stroke, and heart failure. SBP levels of <135 mm Hg were associated with reduced mortality (odds ratio [OR], 0.87; 95% CI, 0.79-0.95), and levels <130 mm Hg were associated with reduced risk of stroke (OR, 0.53; 95% CI, 0.38-0.75). Importantly, although significant adverse events, such as hypotension and hyperkalemia were inconsistently reported across trials, there was a significant increase in the odds of adverse events with SBP below both 135 mm Hg and 130 mm Hg.

The meta-analysis by Reboldi et al. included all antihypertensive trials that enrolled patients with hypertension and diabetes but not impaired fasting glucose, and did a series of stratified meta-analyses and meta-regression analyses to determine the benefit associated with different levels of SBP on myocardial infarction and stroke. Decreasing levels of SBP were associated with increasing benefit in terms of stroke, but not in terms of myocardial infarction. A meta-regression examining the association between the degree of SBP lowering and stroke found that for every 5% reduction in SBP, the risk of stroke was reduced by 13%. Such a linear association between SBP reduction and myocardial infarction risk reduction was not noted.

Both of these reviews were limited by the fact that they did not examine target SBPs but rather SBPs achieved in the context of a clinical trial. Further, these reviews could not control for differences in duration of diabetes or glycemic control. As the Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD BP) trial suggested that an interaction between glycemic control and SBP lowering may exist, the inability to account for differences in diabetes management should be noted.

Although the optimal BP target remains uncertain, these meta-analyses and results from ACCORD BP do not provide any compelling evidence to alter the present recommendation (<130/80 mm Hg). This was mainly supported by the association between SBP levels <130 mm Hg and reduction in stroke on 1 hand, and the increased risk of adverse events, such as hypotension and hyperkalemia with lower SBP targets on the other hand, with the majority of adverse effects associated with SBP <120 mm Hg.

XIII. Adherence strategies for patients

Recommendations
1. Adherence to an antihypertensive prescription can be improved by a multipronged approach (Table 8).

Background. There are no changes to these recommendations for 2012.

XIV. Treatment of secondary hypertension due to endocrine causes

Recommendations
1. Treatment of hyperaldosteronism and pheochromocytoma are outlined in Supplemental Tables S2 and S3.

Background. There are no changes to these recommendations for 2012.

Table 8. Strategies to improve patient adherence

<table>
<thead>
<tr>
<th>Strategy to improve patient adherence</th>
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</thead>
<tbody>
<tr>
<td>Assist your patient to adhere by:</td>
</tr>
<tr>
<td>Tailoring pill-taking to fit patients’ daily habits (Grade D)</td>
</tr>
<tr>
<td>Simplifying medication regimens to once-daily dosing (Grade D)</td>
</tr>
<tr>
<td>Replacing multiple pill antihypertensive combinations with single pill combinations (Grade C)</td>
</tr>
<tr>
<td>Utilizing unit-of-use packaging (of several medications to be taken together) (Grade D)</td>
</tr>
<tr>
<td>Using a multidisciplinary team approach to improve adherence to an antihypertensive prescription (Grade B)</td>
</tr>
</tbody>
</table>

Assist your patient in getting more involved in their treatment by:
- Encouraging greater patient responsibility/autonomy in monitoring their blood pressure and adjusting their prescriptions (Grade C)
- Educating patients and patients’ families about their disease and treatment regimens (Grade C)

Improve your management in the office and beyond by:
- Assessing adherence to pharmacological and nonpharmacological therapy at every visit (Grade D)
- Encouraging adherence with therapy by out-of-office contact (either by phone or mail), particularly during the first three months of therapy (Grade D)
- Coordinating with pharmacists and work-site health care givers to improve monitoring of adherence with pharmacological and lifestyle modification prescriptions (Grade D)
- Utilizing electronic medication compliance aids (Grade D)

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### Table 9. Considerations in the individualization of antihypertensive therapy

<table>
<thead>
<tr>
<th>Hypertension without other compelling indications (target BP &lt; 140/90 mm Hg)</th>
<th>Initial therapy</th>
<th>Second-line therapy</th>
<th>Notes and/or cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diastolic with or without systolic hypertension</td>
<td>Thiazide diuretics, β-blockers, ACE inhibitors, ARBs, or long-acting CCBs (consider ASA and statins in selected patients). Consider initiating therapy with a combination of first-line drugs if the BP is ≥ 20 mm Hg systolic or ≥ 10 mm Hg diastolic above target</td>
<td>Combinations of first-line drugs</td>
<td>Not recommended for monotherapy: α-blockers, β-blockers in those ≥60 years of age, ACE inhibitors in blacks. Hypokalemia should be avoided in those prescribed diuretic monotherapy. ACE inhibitors, ARBs, and direct renin inhibitors are potential teratogens, and caution is required if prescribing to women of childbearing potential. Combination of an ACE-inhibitor with an ARB is not recommended.</td>
</tr>
<tr>
<td>Isolated systolic hypertension without other compelling indications</td>
<td>Thiazide diuretics, ARBs, or long-acting dihydropyridine CCBs</td>
<td>Combinations of first-line drugs</td>
<td>Same as diastolic with or without systolic hypertension</td>
</tr>
<tr>
<td>Diabetes mellitus (target BP &lt; 130/80 mm Hg)</td>
<td>ACE inhibitors or ARBs</td>
<td>Addition of dihydropyridine CCB is preferred over thiazide</td>
<td>A loop diuretic could be considered in hypertensive CKD patients with extracellular fluid volume overload</td>
</tr>
<tr>
<td>Diabetes mellitus not included in the above category</td>
<td>ACE inhibitors, ARBs, dihydropyridine CCBs, or thiazide diuretics</td>
<td>Combination of first-line drugs. If combination with an ACE inhibitor is being considered, a dihydropyridine CCB is preferable to thiazide diuretic</td>
<td>Normal ACR &lt; 2.0 mg/mmol in men and &lt; 2.8 mg/mmol in women</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>ACE inhibitors or ARBs (except in low-risk patients); β-blockers for patients with stable angina</td>
<td>Long-acting CCBs. When combination therapy is being used for high risk patients, an ACE inhibitor/dihydropyridine CCB is preferred</td>
<td>Avoid short-acting nifedipine. Combination of an ACE inhibitor with an ARB is specifically not recommended</td>
</tr>
<tr>
<td>Recent myocardial infarction</td>
<td>β-Blockers and ACE inhibitors (ARBs if ACE inhibitor-intolerant)</td>
<td>Long-acting CCBs if β-blocker contraindicated or not effective</td>
<td>Nondihydropyridine CCBs should not be used with concomitant heart failure</td>
</tr>
<tr>
<td>Heart failure</td>
<td>ACE inhibitors (ARBs if ACE inhibitor-intolerant) and β-blockers. Aldosterone antagonists (mineralocorticoid receptor antagonists) may be added for patients with a recent cardiovascular hospitalization, acute myocardial infarction, elevated B-type natriuretic peptide or N-terminal-proBNP level, or NYHA class II to IV symptoms</td>
<td>ACE inhibitor and ARB combined. Hydralazine/isosorbide dinitrate combination if ACE inhibitor and ARB contraindicated or not tolerated. Thiazide or loop diuretics are recommended as additive therapy, Dihydropyridine CCB</td>
<td>Titrates doses of ACE inhibitors and ARBs to those used in clinical trials. Carefully monitor potassium and renal function if combining any of ACE inhibitor, ARB, and/or aldosterone antagonist</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>ACE inhibitor, ARB, long-acting CCB, or thiazide diuretics.</td>
<td>Combination of additional agents</td>
<td>Hydralazine and minoxidil should not be used</td>
</tr>
<tr>
<td>Past stroke or TIA</td>
<td>ACE inhibitor/diuretic combinations</td>
<td>Combination of additional agents</td>
<td>Treatment of hypertension should not be routinely undertaken in acute stroke unless extreme BP elevation. Combination of an ACE inhibitor with an ARB is not recommended</td>
</tr>
<tr>
<td>Nondiabetic CKD (target BP &lt; 140/90 mm Hg)</td>
<td>ACE inhibitors (ARBs if ACE inhibitor-intolerant) if there is proteinuria. Diuretics as additive therapy</td>
<td>Combinations of additional agents</td>
<td>Carefully monitor renal function and potassium for those taking an ACE inhibitor or ARB. Combinations of an ACE inhibitor and ARB are not recommended in patients without proteinuria</td>
</tr>
<tr>
<td>Renovascular disease</td>
<td>Does not affect initial treatment recommendations</td>
<td>Combinations of additional agents</td>
<td>Avoid ACE inhibitors or ARB if bilateral renal artery stenosis or unilateral disease with solitary kidney</td>
</tr>
</tbody>
</table>
Peripheral arterial disease
- Does not affect initial treatment recommendations

Dyslipidemia
- Does not affect initial treatment recommendations

Overall vascular protection
- Statin therapy for patients with 3 or more cardiovascular risk factors or atherosclerotic disease. Low dose ASA in patients with controlled BP

<table>
<thead>
<tr>
<th>Other conditions (target BP &lt; 140/90 mm Hg)</th>
<th>Initial therapy</th>
<th>Second-line therapy</th>
<th>Notes and/or cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral arterial disease</td>
<td>Does not affect initial treatment recommendations</td>
<td>Combinations of additional agents</td>
<td>Avoid β-blockers with severe disease</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Does not affect initial treatment recommendations</td>
<td>Combinations of additional agents</td>
<td>—</td>
</tr>
<tr>
<td>Overall vascular protection</td>
<td>Statin therapy for patients with 3 or more cardiovascular risk factors or atherosclerotic disease. Low dose ASA in patients with controlled BP</td>
<td>—</td>
<td>Caution should be exercised with the ASA recommendation if BP is not controlled</td>
</tr>
</tbody>
</table>

ACE, angiotensin-converting enzyme; ACR, albumin-to-creatinine ratio; ARB, angiotensin-receptor blocker; ASA, acetylsalicylic acid; BNP, B-type natriuretic peptide; BP, blood pressure; CCB, calcium channel blocker; CKD, chronic kidney disease; NYHA, New York Heart Association; TIA, transient ischemic attack.

*Albuminuria is defined as persistent ACR > 2.0 mg/mmol in men and > 2.8 mg/mmol in women.
†Proteinuria is defined as urinary protein > 500 mg per 24 hours or ACR > 30 mg/mmol.

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Implementation

The implementation task force conducts an extensive knowledge translation effort to enhance uptake and applicability of these recommendations. These efforts briefly include knowledge exchange forums, targeted educational materials for primary care providers, as well as patients, and freely available slide kits and summary documents of all recommendations on the Canadian Hypertension Society Web site (www.hypertension.ca). Documents are available in French and English, and some documents are translated into other languages. The CHEP outcomes task force conducts hypertension surveillance studies and review of existing Canadian health surveys to identify gaps between current and best practices. The implementation task force also regularly receives feedback from end users to improve guideline processes and content. Although the number of primary care providers that directly receive CHEP materials on a regular basis has dramatically increased, CHEP is continuing to address the barrier and challenge of identifying and reaching all active primary care providers across Canada for dissemination of CHEP materials.

Future Directions

The present report (see Table 9 for the summary of pharmacological management of hypertension) represents the 13th iteration of the annually updated CHEP recommendations for the management of hypertension, and we will continue to conduct yearly systematic reviews of the clinical trial evidence to update our recommendations for therapy annually. The prevalence of hypertension in Canada continues to increase and is predicted to reach 7,500,000 people in 2012/2013 with over 1000 people newly diagnosed with hypertension every day. Therefore, there is a need to focus our efforts on prevention of hypertension, which is the CHEP theme for 2012. The overall goal of the CHEP is to improve awareness, treatment, and control of hypertension in Canada.

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Disclosures

Disclosures can be found in Supplemental Appendix S2 available online at www.onlinecj.ca.

References


46. Food and Drug Administration. FDA Drug Safety Communication: No increase in risk of cancer with certain blood pressure drugs – Angiotensine


Supplementary Material
To access the supplementary material accompanying this article, visit the online version of the Canadian Journal of Cardiology at www.onlinecjc.ca, and at doi:10.1016/j.cjca.2012.02.018.