

Hypertension and Stroke: 2005 Canadian Hypertension Educational Program Recommendations

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ABSTRACT: Background: Hypertension is the most important modifiable cause of stroke. The Canadian Hypertension Educational Program, representing Canada's experts in the field of hypertension, publishes annual evidence-based recommendations on the diagnosis and treatment of hypertension. **Methods:** We present the 2005 Canadian Hypertension Educational Program guidelines regarding the management of hypertension in patients with stroke. **Results:** The diagnosis of hypertension should be expedited and can be made as early as the second visit in patients with stroke. Unless contraindicated, a combination of angiotensin-converting-enzyme (ACE) inhibitors and diuretics is the preferred therapy in these patients. A target blood pressure below 140/90mmHg for non-diabetic patients, below 130mmHg/80mmHg for diabetic patients and below 125mmHg/75mmHg for those with renal disease and proteinuria (≥ 1 gram per day) should be reached. Lifestyle interventions may be as effective as medication and should be used in conjunction with medical management. Waist circumference should be less than 102cm for men and 88cm for women. There remains uncertainty about the management of high blood pressure in the context of acute stroke. **Conclusions:** A combination of ACE-inhibitors and diuretics is recommended in hypertensive stroke patients. Blood pressure should be maintained below 140/90 mmHg.

RÉSUMÉ: Hypertension et accident vasculaire cérébral: recommandations canadiennes 2005 du programme éducatif sur l'hypertension. **Contexte:** L'hypertension est la cause modifiable la plus importante de l'accident vasculaire cérébral (AVC). L'hypertension est la cause principale de l'AVC. Le Groupe de travail du Programme éducatif canadien sur l'hypertension (PÉCH) est formé d'experts canadiens dans le domaine de l'hypertension. Il publie à chaque année des recommandations fondées sur des données probantes sur le diagnostic et le traitement de l'hypertension. **Méthodes:** Nous présentons les recommandations 2005 du PÉCH sur la prise en charge de l'hypertension chez les patients ayant subi un AVC. **Résultats:** Le diagnostic de l'hypertension doit être accéléré chez les patients ayant subi un AVC. Il peut même être fait à la deuxième visite d'évaluation de la pression artérielle chez ces patients. Le traitement de choix chez ces patients est l'association d'un inhibiteur de l'enzyme de conversion de l'angiotensine (ECA) et d'un diurétique, à moins qu'il n'existe des contre-indications à ce traitement. Les valeurs cibles de pression artérielle sont de moins de 140/90 mmHg chez les patients qui ne sont pas diabétiques, de moins de 130/80 mmHg chez les diabétiques et de moins de 125/75 mmHg chez les patients atteints de néphropathie ayant une protéinurie (> 1 gr par jour). Les interventions axées sur le mode de vie peuvent être aussi efficaces que la médication et devraient être utilisées en association avec la médication. Le tour de taille devrait être de moins de 102 cm chez l'homme et de moins de 88 cm chez la femme. La prise en charge d'une pression artérielle élevée dans le contexte d'un AVC aigu demeure controversée. **Conclusions:** L'association d'un ECA et d'un diurétique est recommandée chez les patients ayant subi un AVC et la pression artérielle devrait être maintenue sous 140/90 mmHg.

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Stroke is the leading cause of disability in North America and the third leading cause of death.¹ Hypertension is well recognized as the most important modifiable risk factor for both ischemic stroke and intracerebral hemorrhage.² A significant number of Canadians have one or more major risk factors for stroke. More than 50% of Canadians aged from 55 to 74 years old are hypertensive.³ More than 160,000 people in the United States in 2001 had a fatal stroke and about 540,000 more people suffered a non fatal stroke in the same period.¹ A recent population-based study using an administrative health database showed an incidence of stroke in urban and rural Alberta of 132.4 /100,000 population/year and 138.2/100,000 population/year respectively.⁴ For males over 80 years old, the incidence of stroke reaches 500/100 000 population/year.⁴ In

North America, the direct cost of stroke is estimated to exceed \$57 billion a year.¹

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Health Agency of Canada and the Heart and Stroke Foundation of Canada. It represents Canadian experts in the field of hypertension and provides annual evidence-based recommendations regarding the diagnosis and treatment of hypertension. This year marks the sixth consecutive year that the CHEP has updated its guidelines.

As neurologists, we are commonly faced with patients having both cerebrovascular diseases and high blood pressure. In this article, we present the 2005 CHEP recommendations for hypertension from a stroke perspective.

METHODS

The 2005 CHEP recommendations process incorporated all trials and epidemiological observational studies published in the past 12 months relevant to hypertension. The interpretation/impact of these studies was considered in the context of the cumulative evidence of past publications. For 2005, we incorporated the SHEAF Study,⁵ the Ohasama Cohort,^{6,7} the OvA Study,⁸ Staessen et al.,⁹ Thijs et al.,¹⁰ VALUE,¹¹ ACTION,¹² INVEST¹³ and VALIANT,¹⁴ as well as a range of smaller studies and systematic reviews (particularly the Blood Pressure Lowering Treatment Trialists Collaboration¹⁵ and the calcium channel blockers meta-analysis¹⁶). The CHEP guidelines are based solely on efficacy data and do not include physicians/experts preferences and cost-effectiveness analysis.

RECOMMENDATIONS

Diagnosis and technique

The diagnosis of hypertension should be expedited (Figure).

Past guidelines required a minimum of three visits with a blood pressure (BP) > 140/90mmHg to make the diagnosis of hypertension in patients with target organ damage, including stroke or transient ischemic attack. Although minimizing the risk of misdiagnosing patients as hypertensive, such a conservative approach is not practical given the realities of health care delivery in Canada and is no longer appropriate. There is accumulating evidence that delaying treatment may expose high risk hypertensive patients to undue risk of hypertensive complications (CAPP,¹⁷ ALLHAT,¹⁸ VALUE¹¹). In these studies, it was suggested that early differences in secondary endpoints between treatment regimens were due to differences in the early extent of blood pressure control. It has also been shown that the risk of stroke begins to increase at a blood pressure as low as 115/75 mmHg.¹⁶ Therefore, the 2005 recommendations necessitate only two visits in patients with target organ damage such as stroke, diabetes or chronic kidney disease. The diagnosis may still be made confidently at the first visit in those presenting with a hypertensive crisis.

Although an office-based technology is most often used by neurologists and other physicians for the diagnosis of hypertension, there is concern about the measurement of blood pressure in this setting. Patients may suffer from the “white coat hypertension”, even with careful attention to technique. Patients are instructed to avoid caffeine one hour prior to and smoking 30 minutes prior to the blood pressure measurement. An appropriate cuff size is essential. Measurement should be undertaken after five minutes rest. Blood pressure should initially be evaluated in both arms and at least twice on the side with the highest value. It is now firmly established that other modalities are as, or more effective, in the measurement/evaluation and prognostic determination of blood pressure elevations, than the clinic evaluation.⁵⁻¹⁰ These modalities include automatic blood pressure monitoring and self/home monitoring. Using these techniques, a threshold of 135/85 mmHg is used for the diagnosis of hypertension with self measurement of blood pressure and daytime ambulatory monitoring instead of 140/90mmHg. A 24-hour ambulatory monitor result ≥ 130/80 mmHg is also considered elevated. Well-calibrated/validated equipment is mandatory. Patients and practitioners (for automatic blood pressure monitoring) should be properly educated about the technical aspects of blood pressure measurement. Patients buying their sphygmomanometer at the pharmacy should look for a logo on the packaging, ensuring that this device meets the international standards (British Hypertension Society, International Protocol, Association for the Advancement of Medical Instrumentation) for accurate blood pressure measurement.

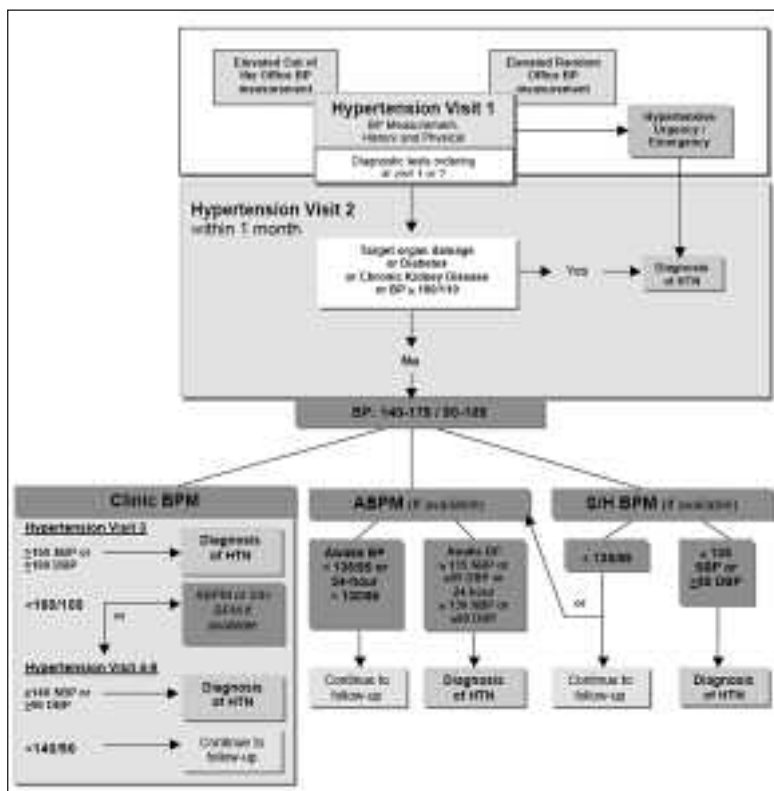


Figure: The expedited assessment and diagnosis of patients with hypertension: focus on validated technologies for blood pressure assessment. ((BPM = blood pressure monitoring, ABPM = Ambulatory blood pressure monitoring, S/H BPM = self/home blood pressure monitoring)

Table 1: Hypertension causes*

| |
|--------------------------------------------------------------------------|
| Essential hypertension |
| Renovascular hypertension |
| Chronic renal failure or disease, including polycystic kidney disease |
| Acute renal failure |
| Medications (NSAIDs, ASA, corticosteroids, contraceptive pills, etc) |
| Over the counter products (i.e containing ephedrine or pseudo-ephedrine) |
| Hyperaldosteronism |
| Cushing syndrome or disease |
| Pheochromocytoma |
| Sleep-apnea syndrome |
| Bad lifestyle habits (excessive alcohol or salt intake, obesity, etc) |

*Only some causes of hypertension are mentioned

Investigations

All hypertensive patients should have baseline investigations, including: complete blood count, urinalysis, blood chemistry (creatinine, electrolytes), a fasting glucose, a fasting lipid profile and a 12-lead echocardiogram (ECG) (looking for left ventricular hypertrophy or evidence of past myocardial infarction). An echocardiogram is not recommended routinely. A renal ultrasound is performed (to exclude an obstruction, polycystic kidney disease or evaluate kidneys size) in those with increased creatinine, renal disease or proteinuria. Stroke patients with hypertension presenting with spontaneous or profound diuretic-induced hypokalemia (< 3mmol/L), refractory high blood pressure or incidental adrenal adenomas should be investigated for primary hyperaldosteronism (morning sample of

plasma renin and aldosterone). Uncontrolled hypertension (≥ 3 drugs), deteriorating renal function or recurrent episodes of pulmonary edema suggest renovascular hypertension and patients should be further evaluated.

Lifestyle modifications

Lifestyle modifications are the cornerstone of the “global” management of many atherosclerotic risk factors, including hypertension (Table 2). Modern western societies discourage physical activity resulting in an epidemic of obesity in North America.¹⁹ Even brief physician and dietician interventions have proven beneficial in hypertensive patients.²⁰ Exercising 30 to 60 minutes four to seven days a week (i.e., walking) will reduce the possibility of becoming hypertensive and reduce blood pressure in those already hypertensive (as well as having beneficial effects on serum lipids).²¹ Therefore, lifestyle modifications should be encouraged even before the development of hypertension in patients with stroke. A well-balanced and healthy diet, including a large quantity of fruits/vegetables and a low quantity of saturated fat is advised.^{22,23} A daily salt intake below 100mmol/L is recommended, especially in those considered salt-sensitive: Canadians of African descent, patients over 45 years old, individuals with impaired renal function or with diabetes. Moderation of alcohol intake (≤ 14 drinks/week for men and $\leq 7-9$ drinks/week for women) is advocated as is cessation of cigarette smoking. Keeping the waist circumference less than 102 cm for men and 88 cm for women will reduce the possibility of becoming hypertensive and developing the metabolic syndrome.²⁴ *Each lifestyle modification is approximately as effective in reducing blood pressure as one prescribed medication.*^{20,21,23,24} Neurologists as well as other physicians should be proactive in promoting healthy lifestyles in patients with stroke.

Table 2: Lifestyle modifications

| <i>Lifestyle component</i> | <i>Recommendations</i> |
|----------------------------|------------------------------------------------------------------------------------------------------------|
| Alcohol intake | $\leq 7-9$ drinks/week for women ≤ 14 drinks/week for men |
| Exercise | ≥ 4 periods of 30-60 minutes/week |
| Salt intake | ≤ 100 mmol/day* |
| Diet | DASH diet (large quantity of fruits, vegetables and low fat dairy product, low quantity of saturated fat)† |
| Waist circumference | < 102 cm for men < 88 cm for women |
| Body Mass Index (BMI) | 18.5-24.9 kg/m ² |
| Smoking | Cessation or abstinence |

*Salt intake restriction is especially recommended in salt-sensitive individuals: Canadians of African descent, age over 45, individuals with impaired renal functions or with diabetes. †DASH (Dietary Approach to Stop Hypertension)

Table 3: Target values for blood pressure (secondary prevention in patients with stroke)

| <i>Condition</i> | <i>Target (SBP/DBP mmHg)*</i> |
|---------------------------------------|-------------------------------|
| Diastolic \pm systolic hypertension | <140/90 |
| Isolated systolic hypertension | <140 |
| Diabetes | <130/80 |
| Renal disease | <130/80 |
| Proteinuria > 1g/day | <125/75 |

*Systolic blood pressure/diastolic blood pressure

Pharmacological treatment

Stroke is considered evidence of target organ damage. The targets for BP control are not specifically different for stroke patients [Table 3]. Blood pressures at least lower than 140/90 mmHg should be obtained in all patients. Although some data suggest that an increased risk of stroke begins as the blood pressures rises above 115/75mmHg,¹⁶ there has been no randomized controlled trial (in patients with stroke) aiming for blood pressure as low as 120/80mmHg or showing a benefit by reducing blood pressure to such values.

Preventing hypertension-related complications in the "general" population of patients with hypertension is more dependent on the extent of blood pressure lowering achieved than on the choice of any specified "first-line drug". Any of the five drug classes shown to reduce cardiovascular outcomes in hypertensive individuals is an appropriate choice for first line monotherapy in hypertensive patients. Thiazide diuretics, long-acting calcium channel blockers, beta-blockers (in patients younger than 60 years), angiotensin converting enzyme inhibitors (ACEI) (in non-blacks), angiotensin receptor blockers (ARBs) are all acceptable first-line therapies. The new inclusion of longer-acting nondihydropyridine agents reflects the accumulating evidence, including a systematic review demonstrating the comparable effectiveness of both dihydropyridine and nondihydropyridine agents in reducing hypertension-related complications.¹⁶

For secondary prevention in patients with stroke and hypertension, the current literature suggests that a combination of an ACE inhibitor and a thiazide diuretic is the preferred therapy. For those with contraindications, other classes of medications mentioned above may be used. Although all classes of agents have been proven efficacious in preventing stroke among hypertensive patients, only one randomized controlled trial studied exclusively a stroke population at baseline and used stroke as the primary endpoint.²⁵ In the PROGRESS trial, the combination ACE inhibitor/thiazide diuretic was superior to placebo while an ACE inhibitor alone showed no superiority to placebo. This study did not provide a direct comparison with other classes of agents. The Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT) also included patients with stroke but the exact number was not mentioned (23% had either a stroke or a myocardial infarction at

baseline) and the primary endpoint was coronary heart disease mortality/non fatal myocardial infarction.¹⁸ In this study, the primary endpoint was not significantly different between groups. Until a direct comparison between classes of antihypertensive agents in patients with stroke is achieved, a combination of an ACE inhibitor/thiazide diuretic is recommended.

Among patients with stroke, the global cardiovascular risk should also be addressed. Therefore, statins and platelet inhibitors are complementary and essential to any anti-hypertensive strategy and should be considered for all. Note that the beneficial effect of statin therapy among patients who have already suffered a stroke appears largely in reducing cardiac risk rather than reducing future stroke.²⁶

Patients' adherence to therapy, including lifestyle modifications, is an essential component of hypertension management. Noncompliance is an important cause of "resistant" hypertension. Education of the patient and family are critical. Simple regimens (i.e once daily dosing) are preferred. It is important to assess adherence to therapy at each visit (eg. by asking patients and family about medication/life style habits, compliance/side effects, looking at drug bottle pill consumption, etc). Self measurement of blood pressure and strategies to increase self management of hypertension can be effective in improving adherence.

High blood pressure in the setting of acute stroke

High blood pressure is very common at presentation and early after ischemic (75%) or hemorrhagic (>80%) stroke.²⁷ In both cases, this is associated with a poor functional outcome.²⁸ There is a paucity of evidence-based data in the literature and therefore CHEP has not issued explicit recommendations on managing hypertension in acute stroke. Although a phase II study showed the safety of an angiotensin receptor blocker (average time of 30 hours post stroke), there was no significant reduction in blood pressure in the active treatment group.²⁹ The ASA/AHA (American Stroke Association/American Heart Association) recommends treating blood pressures above 220/120 mmHg for ischemic stroke and over 185/105mmHg for hemorrhagic stroke.^{30,31} The CHEP 2005 recommendations do not involve a specific blood pressure range. Because it is unclear how to proceed, a conservative approach is warranted, especially in older patients with ischemic stroke and suspected carotid

stenosis/occlusion. Some conditions associated with stroke necessitate a more aggressive treatment, including aortic dissection, acute myocardial infarction and hypertensive encephalopathy.

In those eligible for intravenous thrombolytic therapy, a blood pressure lower than 185/110 mmHg must be obtained prior and during treatment, based on the NINDS inclusion-criteria.³² Labetalol, being easily titrated and having minimal vasodilatory effects on cerebral vessels, is often used. Short acting calcium antagonists should be avoided because of their rapid absorption and their potential to induce acute hypotension.^{33,34} Clonidine also has the potential of substantially reducing blood pressure and should be used with caution.

Urgent trials concerning the management of high blood pressure and acute stroke are needed. This has been recognized as a priority by the International Society of Hypertension.²⁷ Future research should address the following questions: Should blood pressure be elevated or lowered (with target BP ranges) in patients with ischemic stroke? With hemorrhagic stroke? Which drug classes should be used? When should therapy be initiated? Which subgroups of patients benefit according to: demographics, stroke mechanism, co-morbid conditions, severity of neurological lesions and coexistent medications?

CONCLUSIONS

Hypertension is a significant public health problem in Canada and remains one of the most common and important risk factors for stroke. Blood pressure should be maintained below 140/90mmHg in most patients with stroke. A combination of an ACE inhibitor and a thiazide diuretic is suggested for secondary prevention in these patients. Lifestyle modifications remain the cornerstone of the treatment and prevention of hypertension. Neurologists should be active in the management of this condition, including prescribing medications and counseling stroke patients about their risk factors.

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