Managing hypertension: evidence supporting the 2013/2014 recommendations of the Canadian Hypertension Education Program

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Competing interests: Raj Padwal is a consultant for Forest Laboratories and Medtronic; he received grant funding for clinical trials from NovoNordisk, CVRx and Valencia; he received payment for the development of educational presentations from Abbott, Servier and Merck. No other competing interests were declared.

This article has been peer reviewed.

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***CMAJ* 2015. DOI:10.1503/cmaj.131440**

Each year, the Recommendations Task Force of the Canadian Hypertension Education Program updates its recommendations for the diagnosis and treatment of hypertension in Canada. During the past two years, the task force has made some substantial changes to recommendations in several areas. These include changes to thresholds for starting treatment and blood pressure targets in older adults, as well as changing health behaviours (e.g., resistance training, sodium intake). The task force also looked at the clinical implications of the J-curve phenomenon in patients with coronary artery disease. Here, we summarize the evidence underpinning the updated recommendations. The complete recommendations, including discussion of changes not included here and detailed methods, can be found elsewhere.[1,2]

Synopsis of methods

Systematic literature searches, using text words and medical subject headings, of the MEDLINE and PubMed databases are done annually by a Cochrane Collaboration librarian. Search results pertinent to content areas are reviewed by specific subgroups who determine the importance of the studies and propose changes to recommendations. The evidence is examined by a central review committee with expertise in research methods. The task force meets to discuss proposed recommendations and the supporting evidence. After discussion and modification, a vote is held for each proposed change; a minimum 70% endorsement is needed for a recommendation to be adopted. The Canadian Hypertension Education Program provides a grade to each recommendation based on the strength of the underlying evidence.[3] For example, for recommendations addressing therapy, an A (high) designation requires a randomized controlled trial with definitive results, a clinically important outcome and a representative study population; a D (weak) designation might be given to a recommendation supported by an unvalidated surrogate end point or an inconclusive result subject to interpretation.

Key points

- This article summarizes the evidence behind updates to the 2013 and 2014 Canadian Hypertension Education Program (CHEP) guidelines.
- We review the evidence leading to changes to the recommendations for sodium intake and the threshold for starting pharmacotherapy in older adults.
- We also review the evidence behind two new recommendations regarding target blood pressure levels in patients with coronary artery disease and the use of resistance exercise by patients with hypertension.

Treating hypertension in older adults

Isolated systolic hypertension, defined according to traditional blood pressure targets (≥ 140/90 mm Hg), affects 74% of people aged 80 years or older.[4] Recent publications on hypertension in older adults, including the results of a one-year, open-label, active treatment extension of the original Hypertension in the Very Elderly Trial (HYVET),[5,6] prompted the task force to specifically examine thresholds for starting treatment and therapeutic targets in this population.

Before the publication of the HYVET, a meta-analysis of data from older subgroups from five placebo-controlled randomized trials (1670 people comprising 15% of the total study participants) examined the effect of antihypertensive therapy in older adults. This meta-analysis reported that, compared with placebo, antihypertensive therapy reduced the incidence of stroke

(relative risk [RR] 0.66, 95% confidence interval [CI] 0.48–0.92), major cardiovascular events (RR 0.78, CI not reported; $p = 0.01$) and heart failure (RR 0.61, CI not reported; $p = 0.01$).[7] No definitive effect on all-cause mortality was seen (RR 1.06, 95% CI 0.95–1.18).

The HYVET specifically evaluated the effect of lowering blood pressure in older adults on fatal or nonfatal stroke (the primary outcome).[5] Secondary outcomes included all-cause mortality and cardiovascular mortality. Participants with a systolic blood pressure of 160 mm Hg or more were assigned to target blood pressure levels lower than 150/80 mm Hg (sustained-release indapamide, 1.5 mg once daily, with addition of perindopril 2–4 mg daily if needed). At two years' follow-up, the achieved blood pressure levels were 15.0/6.1 mm Hg lower in the active treatment group than in the placebo group (mean reduction 29.5/12.9 v.14.5/6.8 mm Hg). The trial was stopped early at the recommendation of the data safety and monitoring board. Notably, the prespecified "stopping rule" published in the original protocol was not followed.[8] The final analysis suggested a favourable effect of active treatment on the incidence of stroke, but the results were not definitive (1.2% v. 1.8%; hazard ratio [HR] 0.70, 95% CI 0.49–1.01). There was, however, a significant reduction in all-cause mortality in the active treatment group (4.7% v. 6.0%; HR 0.79, 95% CI 0.65–0.95).

The main trial was followed by a one-year, open-label extension with both arms offered active treatment.[6] Results were inconclusive with respect to stroke outcomes (HR 1.92, 95% CI 0.59–6.22), and a definitive effect on all-cause mortality persisted (47 events; HR 0.48, 95% CI 0.26–0.87). Between-group differences in blood pressure were not clinically important in the one-year extension phase (1.2/0.7 mm Hg higher in group previously receiving placebo), suggesting that blood pressure differences during the main trial were responsible for the benefits seen.

Based on the results of the HYVET trial, the Canadian Hypertension Education Program recommends that the systolic blood pressure threshold for starting drug therapy should be 160 mm Hg or more for older adult patients (age ≥ 80 yr) who do not have diabetes or end organ damage. The program also made a new recommendation that the systolic blood pressure target for this group should be below 150 mm Hg. However, the lack of definitive effect on the trial's primary outcome and the trial's early discontinuation led the task force to assign a C grade to these recommendations (Box 1).

The J-curve phenomenon in patients with coronary artery disease

Concerns have been raised regarding the potential for harm after excessive reduction of diastolic blood pressure in patients with coronary artery disease.[2] Diastolic blood pressure is the major determinant of coronary artery perfusion pressure. Data from patients with hypertension undergoing coronary artery catheterization show that a diastolic blood pressure lower than 60 mm Hg is associated with low myocardial perfusion pressure.[9]

Furthermore, in the Systolic Hypertension in Europe (Syst-Eur) trial, the rate of cardiovascular events increased when diastolic blood pressure was lower than 70 mm Hg (independent of systolic blood pressure) in patients aged 60 years and older who had coronary artery disease and were receiving active treatment for hypertension. This increase in events appeared to reach statistical significance at a diastolic blood pressure value of about 60 mm Hg.[10] These and other data[2] led the task force to introduce a cautionary recommendation that applies only to patients with established coronary artery disease.

The Canadian Hypertension Education Program recommends that when decreasing systolic blood pressure to target levels in patients with established coronary artery disease (especially if isolated systolic hypertension is present), clinicians should be cautious when the diastolic blood

Box 1: Summary of updated recommendations

- In older adult patients (age ≥ 80 yr) who do not have diabetes or end organ damage, the systolic blood pressure threshold for starting drug therapy is 160 mm Hg or higher (revised recommendation, 2014, grade C).
  The target for systolic blood pressure should be less than 150 mm Hg (new recommendation, 2013, grade C).
- When decreasing systolic blood pressure to target levels in patients with established coronary artery disease (especially if isolated systolic hypertension is present), be cautious when the diastolic blood pressure is ≤ 60 mm Hg because of concerns that myocardial ischemia might be exacerbated (new recommendation, 2014, grade D).
- For patients who do not have hypertension or who have stage 1 hypertension (i.e., systolic pressure 140–159 mm Hg, diastolic pressure 90–99 mm Hg), the use of resistance or weight training (such as free weight lifting, fixed-weight lifting, or handgrip exercise) does not adversely influence blood pressure (revised recommendation, 2013, grade D).
- To decrease blood pressure, consider reducing sodium intake toward 2000 mg (5 g salt or 87 mmol sodium) per day (revised recommendation, 2014, grade A).

Note: A = based on high-quality randomized controlled trials with high internal validity, statistical precision and direct applicability to the issue of concern; B = based on randomized controlled trials of lower precision, somewhat different population and validated intermediate or surrogate outcomes; C = based on observational studies or lower quality trials; D = expert opinion.

pressure is 60 mm Hg or higher, because of concerns that myocardial ischemia might be exacerbated (Box 1). Exercising caution involves looking more carefully for signs and symptoms of reduced coronary blood flow, in which case the benefits of further blood pressure lowering will need to be judged against the risks of worsening myocardial ischemia.

Health behaviour modification

Based on recently published meta-analyses, the task force voted to revise two recommendations related to health behaviour, one pertaining to resistance exercise and the other to salt intake.

Resistance exercise

In a meta-analysis of 28 trials examining resistance exercise (dynamic and isometric resistance training, 3 sessions/wk),[11] conclusive reductions in both systolic (3.87 mm Hg, 95% CI 1.5–6.2 mm Hg) and diastolic (3.6 mm Hg, 95% CI 2.1–5.0 mm Hg) blood pressure were reported. Notably, the results were not definitive in the four trials that specifically involved patients with hypertension: although there was a mean reduction of 4.1 mm Hg, the 95% CI extended from a 6.4 mm Hg reduction to 1.4 mm Hg increase.

Many patients with hypertension may avoid this type of exercise because of concerns of elevated blood pressure. Based on the results of this meta-analysis, the task force determined there was evidence that, when performed according to recommended techniques, resistance training does not appear to adversely influence blood pressure (Box 1). However, blood pressure was not the primary outcome in most trials included in the meta-analysis, and important measures of study quality (e.g., randomization procedures, allocation concealment and blinding of outcome assessors) were not described in sufficient detail. Given these limitations in the evidence, this recommendation was assigned a D grade.

Sodium intake

Before 2014, the Canadian Hypertension Education Program recommended daily sodium intakes of less than 1500, 1300 and 1200 mg for adults aged less than 50 years, 51–70 years and more than 70 years, respectively (grade B). This recommendation was updated and simplified in 2014, advising practitioners to consider counselling patients to lowering sodium intake to 2000 mg when the goal is to lower blood pressure (Box 1).

A review by the World Health Organization Nutrition Guidance Expert Advisory Group — Subgroup on Diet and Health[12] included only randomized controlled trials that reported an achieved reduction in sodium intake of at least 40 mmol per day (920 mg sodium or 2.3 g salt) and measured intake using 24-hour urinary sodium excretion. In 24 trials that enrolled 2273 patients with hypertension, a mean reduction in systolic blood pressure of 4.06 mm Hg (95% CI 2.96–5.15) was noted. Diastolic blood pressure was reduced by a mean of 1.38 mm Hg (95% CI 0.02–2.74). Among the 927 patients receiving treatment with antihypertensive drugs, the mean reduction in systolic and diastolic blood pressures were 4.6 (95% CI 2.5–6.6) and 2.1 (95% CI 0.9–3.2) mm Hg, respectively.

A Cochrane review addressed the effect of "modest" reduction in salt intake on blood pressure over periods of four weeks or more.[13] The review included parallel-group and crossover randomized controlled trials. Reductions in 24-hour urinary sodium excretion were required to be within the range of 40–120 mmol (equivalent to a reduction of 920–2758 mg sodium/d or 2.3–7.0 g salt/d). In the 22 trials that involved patients with hypertension (n = 999; random effects model), a 5.39 mm Hg reduction in systolic blood pressure (95% CI 4.15–6.62) and a 2.82 mm Hg reduction in diastolic blood pressure (95% CI 2.11–3.54) were reported in the intervention arms. Given that the baseline median 24-hour urine sodium excretion was 162 mmol (9.5 g salt) and the mean reduction in the active arms was 75 mmol (4.4 g salt), a target daily sodium intake of 87 mmol (equivalent to 2000 mg of sodium or 5 g of salt) was felt to represent a reasonable threshold.

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Contributors: All of the authors contributed to the preparation of the manuscript and agree to act as guarantors of the work.

Funding: The Canadian Hypertension Education Program is operated and funded by Hypertension Canada. K. Dasgupta holds the Fonds de recherche Santé du Québec–Société Québécoise d'hypertension artérielle Jacques de Champlain Award.

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The Canadian Hypertension Education Program guidelines are updated on an annual basis. Further information on the process, timelines, summaries of the recommendations, presentation slide kits and patient education tools are available at www.hypertension.ca.