

Hypertension is a common health concern among older adults and constitutes an important risk factor for cardiovascular disease. Despite its prevalence, it is a constant management challenge. We review four aspects of hypertension management that have been of interest over the past year.

Key words: hypertension, diabetes, drug therapy, gender differences, resistant hypertension

Management of Hypertension among Older Adults: Where Are We Now?

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Introduction

Hypertension is a major contributor to death and disability worldwide.¹ It is an important risk factor for cardiovascular disease and the leading cause of congestive heart failure and stroke.² Data from clinic visits of a cross-sectional population collected between 1986–1992 found that 22% of Canadian adults had hypertension,³ over half of whom were unaware of it at the time of diagnosis. Following implementation of the Canadian Hypertension Education Program (CHEP), a health care professional education program, the rate of patient awareness of hypertension increased by 51% and the rate of drug prescription increased by 66%.⁴

This update will highlight four topics that are germane to the issue of hypertension in this patient population as well as discuss gender differences in hypertension prevalence and treatment.

Isolated Systolic Hypertension

Isolated systolic hypertension (ISH) is the most frequent form of hypertension among older adults. Data from the Framingham Heart Study have shown that the systolic pressure rises and the diastolic pressure falls after age 60 in both normotensive and untreated hypertensive subjects, and that ISH accounts for 65–75% of cases of hypertension among older adults.⁵ The elevation in arterial pulse pressure that is characteristic of this condition is thought to be secondary to

diminished arterial compliance that occurs as a result of degenerative changes in the aorta and possibly endothelial dysfunction.⁶

Treatment of isolated systolic hypertension in older adults has been proven to reduce the incidence of stroke and heart failure.⁷ To achieve this, four different classes of agents—thiazide diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and calcium-channel blockers (CCBs)—are recommended as first-line therapy by the Systolic Hypertension in the Elderly Program (SHEP) guidelines. Beta-blockers should not be used as primary therapy for hypertension among individuals over the age of 60 years because of decreased efficacy. ACEs and ARBs tend to be less effective in older adults due to lower renin levels.

Currently the mainstay of treatment consists of a diuretic combined with additional agents to achieve target blood pressure (BP) levels. Two recent studies have confirmed the role of diuretics in the treatment of ISH. In the first trial, a diuretic, indapamide, was shown to be more selective than an angiotensin II receptor blocker or a calcium-channel blocker for decreasing systolic blood pressure (SBP) and pulse pressure without lowering normal diastolic BP levels, which is thought to have deleterious effects.⁸ In the second study, the cardiovascular mortality of a group of people with ISH with or without diabetes was followed for a mean of 14.3 years. A

chlorthalidone (thiazide-type) treatment program was found to improve long-term outcomes regardless of diabetic status. Those individuals who developed diabetes during the follow-up period had a better prognosis than those with pre-existing diabetes (note that chlorthalidone is not presently available in Canada).⁹ Although often difficult to control, it is imperative to treat ISH and to achieve target BP levels in order to decrease a high risk of cardiovascular complications, including stroke, which can be especially debilitating for older adults (Table 1).

Strategies for Drug Therapy: Monotherapy vs. Low-dose Combination Therapy

Management of hypertension is a problem encountered daily in clinical practice. The classical strategies employed by physicians for blood pressure control are sequential monotherapy or stepwise care with initial monotherapy followed by the addition of other drugs to reach targets. However, most patients will require two or more drugs to achieve targets.¹⁰

Multidrug combinations are thought to be more effective than monotherapy as they serve to offset compensatory mechanisms triggered when a drug is initiated that can limit the efficacy of the medication. Multiple trials in individuals with moderate to severe hypertension have found that low-dose combination therapy is at least as effective as high-dose monotherapy with fewer side effects.^{11–14} For this reason, the Joint National Committee on the Detection, Evaluation and Treatment of High Blood Pressure (JNC-7) recommends initial combination therapy if blood pressure must be lowered more than 20/10 mm Hg. While JNC-7 recommends combining a thiazide diuretic with another drug, combinations of a CCB with a BB or ACE inhibitor have been shown to be effective as well.^{11,15}

Low-dose combination therapy may also be valuable for individuals with milder degrees of hypertension. A study by Andreadis *et al.*¹⁶ found that therapy with low-dose ARBs and CCBs was more

Table 1: Blood Pressure Treatment Targets: Canadian Hypertension Education Program Recommendations

Hypertension with no compelling indications	<140/90 mm Hg
Isolated systolic hypertension	<140/90 mm Hg
Diabetes	≤130/80 mm Hg
Renal disease	≤130/80 mm Hg

Source: Khan *et al.*, 2006.³¹

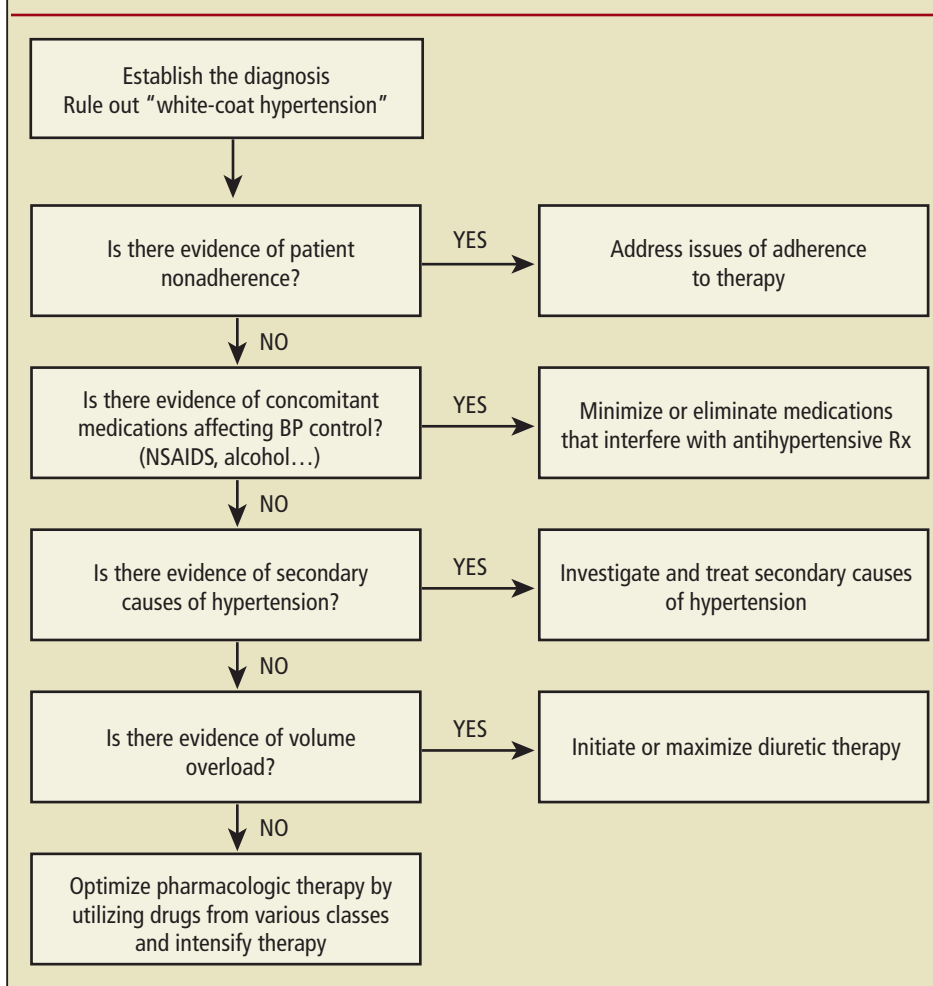
efficacious than high-dose monotherapy for individuals with mild to moderate hypertension (average SBP/DBP 153/97 mmHg) uncontrolled with low-dose monotherapy. Therefore, it may be reasonable to use low-dose combination therapy once low-dose monotherapy fails to reach targets, even in patients with mild to moderate hypertension. Caution must be used whenever combination therapy is commenced for individuals at risk for orthostatic hypotension such as people with diabetes, those with autonomic dysfunction, or adults with pre-existing postural hypotension. Blood pressure should be monitored regularly in both the sitting and standing positions, and volume depletion should be avoided. Combining a beta-blocker with a nondihydropyridine CCB should be avoided to prevent bradycardia. Caution should also be exercised when combining an ACE and ARB, due to potential deterioration in renal function and hyperkalemia. Combining an ACE and ARB is generally not advised for treatment of hypertension, both because of a high risk of hyperkalemia and deterioration of renal function, as well as a lack of evidence for its efficacy.

Hypertension and Diabetes

With up to 60% of people with diabetes affected, concomitant hypertension is an important contributor to the macrovascular complications associated with diabetes.¹⁷ The United Kingdom Prospective Diabetes Study (UKPDS) and Hypertension Optimal Treatment (HOT) trials both demonstrated that intensive treatment of BP to lower targets reduced clinical events.^{17,18} Since thiazide diuretics, ACE

inhibitors, ARBs, BBs, and CCBs have all been shown to improve cardiovascular outcomes, current guidelines stress the importance of achieving BP targets over the use of any specific drug. Results from both the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack (ALLHAT) trial and a meta-analysis by the Blood Pressure Lowering Treatment Trialists' Collaboration confirm this recommendation. Nonetheless, people with diabetes are at high risk for nephropathy, which is a major contributor to morbidity and mortality. Inhibitors of the renin angiotensin system (ACE inhibitors and ARBs) have been shown to slow progression of diabetic nephropathy and reduce the incidence of microalbuminuria compared with CCBs, despite similar reductions in BP.^{19,20} Therefore, these agents should form an integral part of therapy for diabetics, most of whom will require a combination of drugs to achieve targets. In addition, third-generation BBs such as carvedilol and nebivolol may be preferable to second-generation BBs such as metoprolol for people with diabetes.²¹ These drugs offer the cardiac benefits for patients with ischemic heart disease and heart failure, but do not cause the peripheral vasoconstriction and increased insulin resistance that mediate the adverse effects related to BBs among individuals with diabetes.

Numerous studies have demonstrated a decreased incidence of new-onset diabetes among hypertensive patients treated with inhibitors of the renin angiotensin system (ACE inhibitors and ARBs).^{10,22–25} However, the recently published Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) trial

Figure 1: Algorithm for the Management of Resistant Hypertension

found that treatment with ramipril did not decrease the incidence of new-onset diabetes after three years among normotensive patients with impaired fasting glucose or impaired glucose tolerance.²⁶ The discrepancy between these studies may be due to DREAM's lower risk patient population (younger, normotensive, no cardiovascular comorbidities), shorter follow-up, and the control agent being placebo rather than beta-blockers or diuretics, which may predispose to diabetes. Conversely, DREAM was the only trial in which new-onset diabetes was a primary rather than a secondary outcome. Taken together, ACE inhibitors cannot be recommended solely for diabetes prevention; however, they may be preferable in hypertensive patients at high risk for developing diabetes (e.g., those who are obese or exhibit metabolic syndrome).

Resistant Hypertension

Resistant hypertension has recently become the focus of great interest as an issue in the management of hypertension (Figure 1). While the majority of hypertensive patients can achieve adequate blood pressure control with a combination of two to three medications, there is a subset of the population among whom blood pressure control can be refractory to standard medical therapy.

The definition of resistant or refractory hypertension is a blood pressure of $\geq 140/90$ mmHg or $\geq 130/80$ mmHg in patients with diabetes or renal disease despite adherence to treatment with three antihypertensive medications, including a diuretic at adequate doses.²⁷ When diagnosing resistant hypertension, the key is to ensure the absence of "white-coat hypertension" or pseudohypertension.

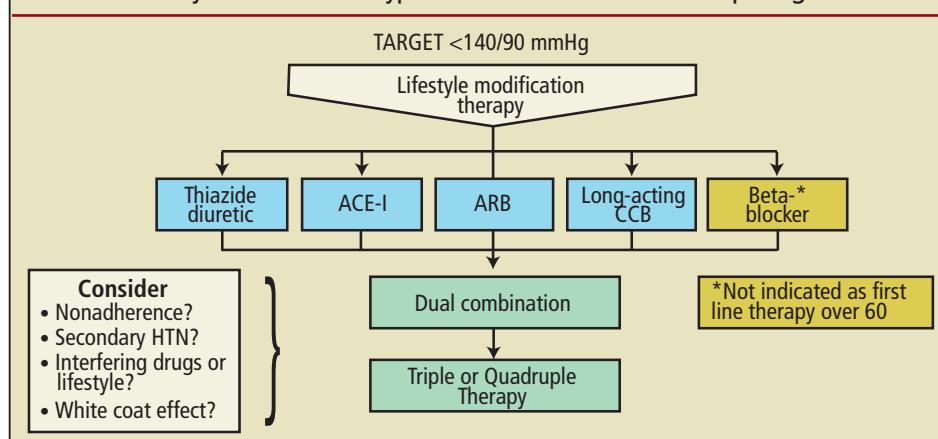
White-coat hypertension is defined as blood pressure readings that are elevated ($>140/90$) during office visits, with out-of-office visits averaging less than 135/85. This phenomenon is due to patient anxiety and is likely to be the cause of disparity between the degree of hypertension and an absence of target-organ damage. This can be overcome with home BP measurements or ambulatory BP monitoring.

Pseudohypertension is a condition that also must be considered when attempting to diagnose resistant hypertension. This occurs in older patients with thickened, calcified arteries. In these cases, compression of the brachial artery with a sphygmomanometer requires a cuff pressure greater than is present within the artery. The net effect, called pseudohypertension, is that the systolic and diastolic pressures estimated from the sphygmomanometer may be considerably higher than the directly measured intra-arterial pressure. The possible presence of pseudohypertension should be suspected if antihypertensive therapy induces symptoms compatible with hypoperfusion (such as dizziness and weakness) in the absence of an excessive reduction in BP, or if there is pipestem calcification of the brachial arteries on radiologic examination. Studies of hypertensive patients with one or more of these findings have found an incidence of pseudohypertension as high as 25%.

In addition, physicians need to pursue strategies that promote their compliance with prescribed treatment regimens as recommended by the Canadian Hypertension Society, found online at www.hypertension.ca/chs/ and outlined in Figure 2.

Resistant hypertension may be due to one of the many secondary causes of hypertension, which should be sought in the event that hypertension is difficult to manage.²⁸ Although the treatment of resistant hypertension is challenging, the focus is on a systematic approach using basic principles.²⁹ These include: one, encouraging lifestyle modification, including weight reduction, regular exercise, and reduced sodium intake; two,

Figure 2: Canadian Hypertension Education Program Recommendations for the Treatment of Systolic-Diastolic Hypertension without Other Compelling Indications



correcting volume overload with diuretic therapy; three, maximizing doses of existing drug therapy; and four, combining drugs from various classes to achieve reductions in volume, sympathetic overactivity, and vascular resistance, as well as to promote smooth muscle relaxation and direct vasodilation.

If hypertension persists despite these measures, referral to a hypertension specialist is recommended.

Gender Differences in Hypertension

There are considerable gender differences in the prevalence of hypertension. Before the age of 50, hypertension is more com-

mon among men than women; however, after the fifth decade of life the incidence of hypertension among women increases sharply to match or even surpass the rates among men.

Although women have higher rates of awareness and treatment, they have lower rates of adequate control. According to the NHANES survey, despite higher treatment rates, only 48% of treated women and 30% of all women had adequate BP control compared with 60% and 33% of treated and all men.³⁰

Both men and women have demonstrated the benefits of antihypertensive therapy in the prevention of cardiovascular disease.⁷ The blood pressure-lowering

effect of the different antihypertensive agents and the outcomes of treatment are generally similar, but some data dictate particular medication choices for women. Beta-blockers tend to be less effective for women than men, while diuretics appear to have added benefit in older women due to increased salt sensitivity.³⁰

In summary, although there are some gender differences in hypertension the message is clear: both men and women benefit from aggressive treatment to achieve target BP levels.



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Key Points

Prompt diagnosis of hypertension and initiation of treatment is important to minimize target organ damage and cardiovascular complications.

Diuretics are a key component in the treatment of isolated systolic hypertension (ISH), but multiple drugs are often needed to manage these difficult-to-control patients.

First-line combination therapy is recommended for moderate to severe hypertension.

Consideration should be given to low-dose combination therapy in mild hypertension if low-dose monotherapy fails.

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are an integral component of blood pressure (BP) control for people with diabetes; however, the focus of management should be on achieving target BP levels rather than the specific agents used.

Once the diagnosis of resistant hypertension has been established, management should focus on eliminating compliance issues and secondary causes, as well as the use of multiclass drug combinations.

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