Blood Pressure and Cardiovascular Disease Risk among Older Adults

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Arterial hypertension is one of the most important and preventable causes of death worldwide; therefore, adequate treatment of high blood pressure should be mandatory for patients with hypertension. Hypertension is defined on the basis of systolic and diastolic blood pressure levels and classified into stages on the basis of the degree of elevation. Normal blood pressure is widely considered as being less than 120/80 mm Hg. The presence of risk factors such as elevated blood cholesterol, smoking, diabetes, and obesity greatly increases the risk for hypertension-related morbid events.

Cardiovascular disease and stroke disproportionately affect older adults. Blood pressure is a potent modifiable target for reducing the risk for stroke and cardiovascular morbidity and mortality in older adults. In clinical trials, the number needed to treat to prevent one cardiovascular death was 79, one fatal or nonfatal stroke was 48, and one fatal or nonfatal coronary event was 64.

Key words: *blood pressure, myocardial infarction, CVA, cardiovascular risk, older adults*

Introduction

Blood pressure (BP)–induced cardiovascular risk rises continuously across the whole BP range. In this article, I review the evidence for the association between uncontrolled high BP and cardiovascular diseases (CVDs) and, in particular, cardiovascular events and cerebrovascular accidents. Classification of blood pressure for adults is presented in Table 1. The World Health Organization (WHO) has reported that suboptimal BP (>115 mm Hg systolic BP [SBP]) is responsible for 62% of cerebrovascular disease and 49% of ischemic heart disease, with little variation by sex. In addition, suboptimal BP is the number one attributable risk for death throughout the world.[2] The JNC-7guidlines classified normal BP to be less than 120/80 as shown in Table 1; however, the WHO report on blood pressure and cardiovascular diseases reported that suboptimal blood pressure control up to levels of >115 mm Hg systolic SBP in patients with hypertension is responsible to increased incidence of cardiovascular disease. JNC-7 recommends no pharmacological therapy for BP <140/90 except for patients with diabetes or renal disease then the cutoff is <130/80.

Prevalence

Hypertension is estimated to cause 4.5% of global disease burden and is as prevalent in many developing countries as it is in the developed world.[1] Worldwide prevalence estimates for hypertension may be as high as 1 billion individuals, and approximately 7.1 million deaths per year may be attributable to hypertension.[2] Data from the National Health and Nutrition Examination Survey have indicated that 50 million or more Americans have high BP warranting some form of treatment.[3,4]

The prevalence of most chronic conditions among adults aged 65 or older did not change significantly between the 1978–1979 Canadian health survey and the 1998–1999 health survey, with the exception of diabetes and asthma, which increased significantly in prevalence (Figure 1).[5]

The Importance of Systolic Blood Pressure

Evidence has accumulated showing the importance of SBP as a major risk factor for CVDs. Blood pressure changes in pattern with increased age. The rise in SBP continues throughout life, in contrast to diastolic blood pressure (DBP), which rises until approximately 50 years of age, tends to level off over the next decade, and may remain the same or fall later in life. Diastolic hypertension is prevalent before 50 years of age, either alone or in combination with systolic hypertension. Systolic hypertension represents the most common form of hypertension: that is why DBP is a more potent cardiovascular risk factor than SBP until age 50; thereafter, SBP is more important.[6]

Clinical Trials and Hypertension

Clinical trials have demonstrated that control of isolated systolic hypertension (ISH) reduces total mortality, cardiovascular mortality, stroke, and heart failure events.[7] ISH is used throughout the article when discussing uncontrolled high BP, unless specified otherwise. Data from studies suggest that poor SBP control is the main reason for the low rates of overall BP control.[8,9] In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) and the Controlled Onset Verapamil Investigation of Cardiovascular End Points (CONVINCE) trial, DBP control rates exceeded 90% but SBP control rates were considerably less (60–70%).[10]

Most physicians have been taught that DBP is more important than SBP and thus treat accordingly. According to one survey of primary care physicians, three-fourths of them failed to initiate antihypertensive therapy in older individuals with an SBP of 140–159 mm Hg, and

most primary care physicians did not pursue control to <140 mm Hg.[11]

Data from eight trials and approximately 105,700 patients >60 years of age with ISH (SBP >160 mm Hg and DBP <95 mm Hg) were analyzed according to treatment versus no treatment. Untreated elevated SBP was shown to be a more important predictor of mortality and cardiovascular complications than untreated elevated DBP. The authors were referring to results of a previous overview. Antihypertensive treatment reduced total mortality across all trials by 13% ($p = .02$), cardiovascular mortality by 18% ($p = .01$), stroke by 30% ($p < .0001$), and coronary events by 23% ($p = .001$).[12]

The number needed to treat to prevent one cardiovascular death was 79, one fatal or nonfatal stroke was 48, and one fatal or nonfatal coronary event was 64. Comparing other health preventive strategies to controlling BP, with mammograms for women between the age of 50–70 years old, the NNT is 270, and it goes higher to 2,500 in women below the age of 50 with no other risk factors.[13] In the three trials that focused exclusively on ISH (the authors of this meta-analysis separated out patients with ISH from the other five trials), antihypertensive treatment decreased total mortality by 17% ($p < .008$), cardiovascular mortality by 25% ($p = .005$), stroke by 37% ($p < .001$), and coronary events by 25% ($p < .001$).

Managing systolic hypertension should become a priority to all physicians to improve the rates of cardiovascular and renal diseases as the population is aging and the toll of uncontrolled SBP will be more pronounced.

The Correlation between Blood Pressure and Myocardial Infarction

Hypertension is a significant, strong, and independent risk factor for coronary artery disease morbidity and mortality, and the reduction of events and mortality by antihypertensive treatment is well documented.

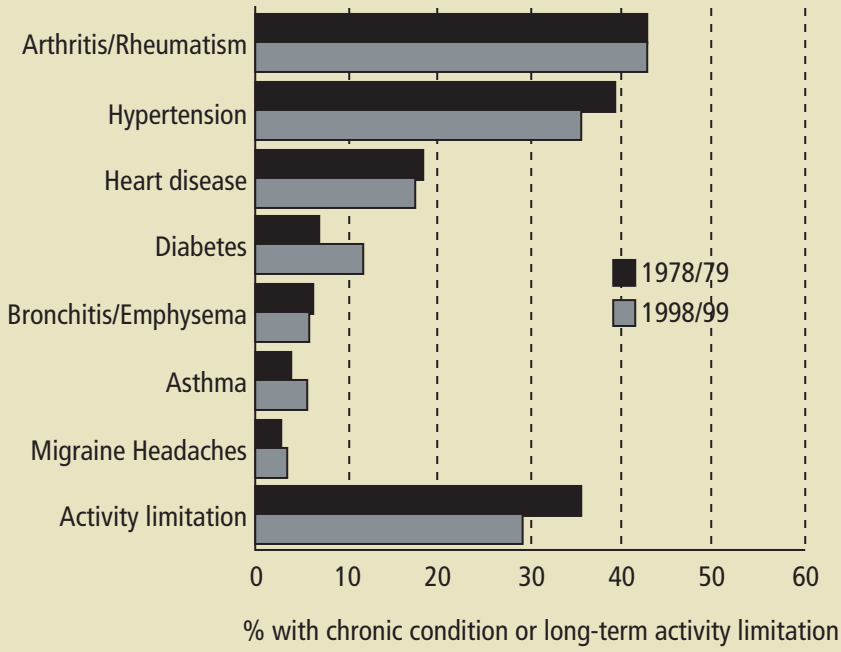
Because of the increase in life expectancy, coronary heart disease is an increasing cause of morbidity and mortality among older adults. Trials in individuals have shown that treatment of hypertension and the use of antithrombotic agents, antagonists, angiotensin-converting enzyme inhibitors (ACEIs), and statins play important roles in the primary and secondary prevention of ischemic heart disease.

A correlation between SBP and death from CVD was demonstrated in the landmark Multiple Risk Factor Intervention Trial, which enrolled 347,978 men aged 35–57 years old.[13] Follow-up at 12 years revealed that SBP was positively linked to a significant risk of cardiovascular mortality both in patients with diabetes and in patients with no diabetes men ($p < .001$). The age-adjusted death rate per 10,000 person-years increased from 53.6 to 242.6 as SBP rose from <120 to ≥200 mm Hg among men with diabetes. Among those without diabetes, the rate rose from 12.2 to 128.7 per 10,000 person-years. At every level of SBP, the mortality rate was markedly higher among diabetic than nondiabetic men. A multi-

Table 1: Classification of Blood Pressure for Adults

Classification	Systolic		Diastolic
Normal	<120	*and*	<80
Prehypertension	120–139	*or*	80–90
Stage 1 hypertension	140–159	*or*	90–99
Stage 2 hypertension	≥160	*or*	≥100

Figure 1: Prevalence of Chronic Conditions or Long-Term Activity Limitation, Household Population Aged 65 or Older, in Canada, Excluding Territories, 1978–1979 and 1998–1999



*Significantly different from 1978–1979 results, p < .05.
Sources: 1978–1979 Canada Health Survey; 1998–1999 National Population Health Survey.[5]

variate regression analysis showed that a 20 mm Hg–higher SBP was associated with a relative risk of 1.60 for nondiabetic and 1.41 for diabetic men, whereas a 20 mm Hg–lower level was associated with relative risks of 0.63 and 0.71, respectively.

Associations between hypertension and CVD were examined in the Strong Heart Study, which collected data on 4,549 Native Americans.[14] After adjustment for all other risk factors, individuals with pretreated, untreated, controlled, and uncontrolled hypertension had approximately 1.74, 1.81, 2.10, and 2.77 times higher risks, respectively, for the development of CVD when compared with normotensive individuals.

The Blood Pressure Lowering Treatment Trialists' Collaboration conducted a meta-analysis of 29 randomized trials (N = 162,341) to investigate the effects of hypertension treatment on CVD events.[15] Specifically, they analyzed studies of the following seven treatment regimens: (1) regimens targeting different BP goals (more intensive versus less intensive goals); (2) calcium channel blocker (CCB) regimens versus placebo; (3) angiotensin receptor blocker (ARB) versus control regimens; (4) ACEI regimens versus placebo; (5) ACEI versus diuretic or beta-blocker regimens; (6) ACEI versus CCB regimens; and (7) ACEI versus ARB regimens.

The investigators found that lower BP targets produced greater relative risk reductions of total major cardiovascular events, as did the CCB-, ARB-, and ACEI-based regimens. For every outcome analyzed (major cardiovascular events, coronary artery disease, heart failure, stroke, cardiovascular death, and total mortality) except heart failure, the differences between the randomized groups in achieved BP reduction were directly associated with the differences in relative risk. No significant differences in total major cardiovascular events were observed between regimens based on ACEIs, CCBs, diuretics, or beta-blockers. Most importantly, fewer cardiovascular events occurred when BP was lowered by any commonly used regimen.

Blood Pressure and Cerebrovascular Accidents

Among individuals with ISH and those with intracranial atherosclerotic disease, BP lowering has consistently been shown to be well tolerated and effective in reducing the risk for stroke and its complications.

Risk Factors

Many modifiable risk factors for cerebrovascular accidents have been identified. Hypertension is a major modifiable risk factor for stroke, and it is the most prevalent and powerful across age, sex, and geographical regions.[16]

Hypertension is risk factor for hemorrhagic and ischemic stroke; also it may be associated with increasing cognitive dysfunction among older adults.[17] Some studies identify hypertension as a risk factor for increased cognitive impairment after stroke. Hypertension is associated with increased risk for vascular cognitive impairment due to small-vessel disease.

Risk Reduction

Risk reduction is a key in preventing stroke and reducing its burden, and BP presents a potent modifiable target. An early meta-analysis of randomized clinical trials measuring the effect of short-term BP lowering among older adults on major coronary events, stroke, and mortality demonstrated a mean treatment effect of 15/6 mm Hg, associated with a relative risk of 0.65 ($p < .005$) for fatal and nonfatal stroke.[18] Several major, large, multicentre, randomized clinical trials have demonstrated the efficacy of treating hypertension and ISH among older adults. The Systolic Hypertension in the Elderly Program, a randomized, placebo-controlled trial enrolling 4,736 individuals age ≥60 years and using a stepped approach to BP control with chlorthalidone with or without atenolol, demonstrated effective BP lowering with a relative risk of 0.64 ($p = .0003$) for total (fatal and nonfatal) stroke, as well as decreased cardiovascular mortality over 5 years.[19] Subsequent analysis of the incidence of stroke subtype (hemorrhagic, ischemic including lacunar, embolic, atherosclerotic) in 4,736 older adults achieving the BP reduction goal of 20 mm Hg demonstrated risk reduction for all stroke subtypes.[20]

The Swedish Trial of Hypertension in Older Patients–2 enrolled 6,614 persons age 70–84 years in this prospective, randomized, clinical trial. The study investigated the efficacy of treatments in reducing cardiovascular mortality and morbidity, demonstrated similar BP reductions in both drug regimen groups, beta-blockers/diuretics versus ACEIs/CCBs, with similar reductions in fatal and nonfatal stroke, and concluded that BP lowering was of major importance in preventing cardiovascular events. A subsequent analysis of a subgroup of 2,280 people with ISH again demonstrated effective BP lowering with no significant difference between the treatment groups, but found a 25% reduction in stroke (driven by a reduction in nonfatal stroke) in patients receiving drugs (ACEIs, CCBs).[21]

Treating Systolic Hypertension

As per all the studies previously mentioned, controlling BP is an essential element to reducing the burden of cardiovascular events. So what is the threshold for BP reduction?

A meta-analysis of 61 prospective observational studies evaluated individual data from one million adults with no previous vascular disease at baseline to assess the relevance of usual BP to vascular mortality. The mortality rate from ischemic heart disease and stroke doubled for every 20 mm Hg increase in usual SBP from ages 40 to 69 years. There was a continuous relationship between usual BP and the risk of mortality from vascular disease, without evidence of a threshold down to 115/75 mm Hg.

The control of systolic hypertension is inadequate, despite the mounting evidence that hypertension treatment in the older adult population decreases all-cause mortality, cardiovascular mortality, and stroke. Isolated systolic hypertension is the most common subtype of uncontrolled hypertension, present in 65% of patients with untreated or inadequately

Key Points

- Hypertension is an epidemic and prevalent chronic medical condition.
- BP control is still not adequate among many older adults.
- Untreated elevated systolic BP is a more important predictor of mortality and cardiovascular complications than untreated elevated diastolic BP.
- Resistant hypertension can require 3 or more agents for adequate control; refer to specialist if BP is still not controlled.

treated hypertension and reaching a frequency of 87% among persons in the sixth decade of life.

Reasons for poor BP control in older persons are complex. A survey of a large health care system reported that many physicians were willing to tolerate an elevated SBP in patients.[22] On average, physicians were initiating drug therapy for SBP at levels >150 mm Hg; in contrast, a DBP of 91 mm Hg or higher prompted therapy. Only 38% of patients whose hypertension had been documented for at least 6 months had therapy initiated or changed. Physicians treating older patients may be reluctant to pursue intensive therapy due to concerns about adverse events. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) states that treatment approaches for older patients should follow the same principles as for younger patients.[16]

According to JNC 7, initiating therapy with two drugs, either separately or in a fixed-dose combination, should be considered for patients with an SBP > 20 mm Hg above the desired goal of <140 mm Hg (or <130 mm Hg for persons with diabetes mellitus or renal disease), particularly those at high risk for cardiovascular events.[16] A thiazide-type diuretic should be one component of the combination drugs; however, other combinations may be appropriate in selected patients, including older adults. The use of combination therapy may increase the likelihood of attaining BP goals, and combinations may also allow lower doses of the component agents to be used, which can result in reduced dose-dependent adverse effects than with higher-dose monotherapy.[15]

As general rules, the simpler the drug regimen, the more likely it is that patients will follow it correctly; and the fewer pills to be taken, the more likely it is that patients will adhere to the regimen. A once-daily antihypertensive drug is particularly relevant for older persons, who may be taking several medications for multiple concomitant medical conditions. Better patient acceptance and adherence to therapy could lead to improved outcomes.

Resistant Hypertension

The definition of resistant hypertension is BP ≥140/90 mm Hg despite treatment with at least three drugs (including a diuretic) in adequate doses and after exclusion of spurious hypertension such as isolated office hypertension and failure to use large cuffs on large arms.

Causes

Causes of resistant hypertension are a failure to modify lifestyle, including weight gain and heavy alcohol intake (binge drinking); poor adherence to the therapeutic plan; continued intake of drugs that raise BP (cocaine, glucocorticoids, nonsteroidal anti-inflammatory drugs, etc.); obstructive sleep apnea; an unsuspected secondary cause; irreversible or limited reversibility of organ damage; and volume overload due to inadequate diuretic therapy, progressive renal insufficiency, high sodium intake, or hyperaldosteronism.

Treatment of Resistant Hypertension

An investigation of causes of resistant hypertension is an essential step in the workup and treatment. Treatment should involve the use of more than three drugs, including an aldosterone antagonist.

Patient Follow-Up

Patients at low risk or with stage 1 hypertension may be seen every 6 months, and regular home BP measurements may further extend this interval. Visits should be more frequent in high or very high risk patients. This is the case also in patients under nonpharmacological treatment alone and in patients who require medication dose titration and the start of new medications.

Conclusion

Individuals with hypertension are at particularly high risk for cardiovascular events, including myocardial infarction, stroke, and their sequelae. BP lowering has consistently been shown to be well tolerated and effective in reducing the risk for cardiovascular events.

Starting therapy with two drugs, either separately or in a fixed-dose combination, should be considered in patients with an SBP >20 mm Hg above the desired goal of <140 mm Hg (or <130 mm Hg for persons with diabetes mellitus or renal disease), particularly in those at high risk for cardiovascular events.

Close follow-up is essential to achieve good BP control while adjusting medications. Referral to a hypertension specialist should be initiated for those with resistant hypertension if BP is not controlled despite three or more BP medications, including a diuretic.

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