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Cardiovascular Care for Older Adults · Open Access ·

Cardiovascular care for older adults: hypertension and stroke in the older adult

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1 Introduction

Hypertension and cerebrovascular disease incidence and prevalence rise dramatically with age, owing to longer exposure time to age-associated alterations in vascular function and structure and cardiovascular risk factors. This chapter is aimed at connecting age-related alterations in vascular function and structure to the resultant target organ damage, and to raise awareness of unique presentations and treatment strategies for hypertension and stroke in older adults.

Much of this chapter builds on the unique physiology of the older adult, as previously described by Dai, *et al*.,[1] and applied to the conditions of hypertension and stroke here. Arterial changes with aging include increased calcium deposition, collagen content, and collagen cross-linking, increased intima-media thickness, increased reactive oxygen species and a pro-inflammatory state and increased apoptosis of vascular smooth muscle cells. These changes lead to stiffer vessels that demonstrate less systolic compliance and diastolic elasticity, increased pulse wave velocity, and increased pulse pressure. The early reflected wave and augmented systolic pressure characteristic of arterial stiffness create greater demands on the left ventricle, resulting in left ventricular hypertrophy and impaired relaxation, which ultimately lead to increased left atrial pressure and size. Coupled with changes in endothelial function, neurohormonal regulation and renal function, these hemodynamic processes create the unique physiology of the older adult, manifest by isolated systolic hypertension, target organ damage and cardiovascular disease (CVD).

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2 Hypertension

2.1 Diagnosis and evaluation

The age-associated increase in large artery stiffness is the major determinant of hypertension in the older adult,[1] making hypertension nearly ubiquitous in those over age 80. In the Framingham Heart Study, the lifetime risk of a healthy 55-year-old individual for developing hypertension was 90%.[2] Both incidence and prevalence of hypertension rise with age, such that 80% of 80-year-old individuals meet criteria for hypertension, and hypertension prevalence approximates age in the US population.[3]

Augmentation of early reflected waves coupled with increased pulse wave velocity and large artery stiffness produce a widened pulse pressure, resulting in isolated systolic hypertension (ISH). ISH is defined by two correctly measured systolic blood pressures (SBP) > 140 mmHg and diastolic blood pressures (DBP) < 90 mmHg. ISH is the most common form of hypertension in older adults, and the combination of increased SBP and reduced DBP seen in ISH is a robust predictor of CVD outcomes in this population.[4] Thus, pulse pressure should be considered in the risk assessment of the older adult, as cross-sectional studies have demonstrated that elevated pulse pressure poses a greater risk for ischemic heart disease than elevated SBP or DBP alone.[5] Importantly, many large randomized controlled trials have demonstrated reduction in risk for major CVD events from lowering SBP in the older adult population.[6–10] It is important for older adults to understand that while arteries stiffen and hypertension is common in their age group,

treatment of elevated blood pressure (BP) reduces their coronary and stroke risk and helps to maintain their functional ability and independence.

The diagnosis of hypertension requires repeated and careful measurement of BP, and this is especially important in the older adult. Owing to alterations in natriuresis, sympathetic activity, and ventricular-vascular stiffening, the older adult is more susceptible to BP variations. BP is correctly measured in the office setting with correct posture and positioning. The patient should be seated comfortably for 5 minutes with his or her back well supported and the arm supported at the level of the heart before the first BP is taken. The patient's feet should touch the floor and legs should not be crossed. The patient should not have smoked or ingested any caffeine within 30 min prior to the BP determinations. BP should be measured with an appropriate sized cuff, preferably with an automated oscillometric device to minimize observer bias. The device should be programmed to wait 5 min before the first BP is taken. Ideally, the examiner should leave the room during the 5 min rest period. BP and heart rate should be measured 3 times at 1 min intervals and the 3 readings be averaged to determine the patient's BP for that particular visit. Hypertension in older adults is generally defined by SBP ≥ 140 mmHg or DBP ≥ 90 mmHg over two clinic visits.

Owing to lower baroreceptor sensitivity, increased sympathetic nervous system activity, and ventricular-vascular stiffening, the older adult is more susceptible to labile BP and orthostatic or post-prandial hypotension. When making treatment decisions, it is important to measure both seated and standing BPs to avoid overtreatment and development of orthostatic hypotension. Because the presence of subclavian stenosis can lead to falsely low BP readings in one arm and possibly result in under-treatment, it is also important to measure BP in both arms on the initial assessment, using the higher of the two arms for treatment decisions and subsequent assessments. Furthermore, differences in upper-arm BP have been shown to independently correlate with CVD risk and can identify patients with subclavian stenosis, peripheral arterial disease, and higher overall risk for CVD. In a meta-analysis, CVD mortality was increased by 70% in patients with an inter-arm difference of ≥ 15 mmHg.[11]

2.2 Treatment

Management of hypertension in older adults requires a comprehensive approach that includes patient education, lifestyle management, and medications. Education includes clear explanation of the relationship of BP to target-organ damage and CVD outcomes and the preventive value of BP control. There was a log-linear relationship between observed SBP and CVD outcomes, including stroke, ischemic heart disease, and overall mortality, in the ≥ 80 year-old participants in the Prospective Studies Collaboration.[12] Since the outcomes of treatment are prevention of events, placing BP elevations and goals in the context of health problems that might affect independence can be very helpful. Also, the provider should discuss the ubiquitous nature of hypertension, natural history of SBP, and potential need for multiple medications when embarking on a treatment pathway.

Non-pharmacologic lifestyle therapy for hypertension is a mainstay in the treatment of all hypertensive individuals. Prevention of hypertension in older adults requires risk factor modification starting early in the life span, including exercise, avoiding smoking, and dietary modifications. Dietary risk factors contributing to the development of hypertension include high sodium intake, inadequate potassium intake, and excessive alcohol consumption. As an adjuvant to medical therapy, sodium reduction, exercise, and weight loss should be recommended to most patients.

Five major randomized controlled trials have tested the effects of BP lowering with pharmacologic therapy on CVD outcomes in older adults. The first of these, the Systolic Hypertension in the Elderly Program (SHEP), randomized 4735 persons aged 60 years and above with ISH (mean baseline SBP 170 mmHg) to active treatment or placebo.[6] The target SBP was 140–160 mmHg, depending on the participants' baseline pressure. After 4–5 years of follow up, stepped-care treatment beginning with a low-dose chlorthalidone with atenolol added if needed reduced total stroke (primary endpoint) by 36% and major CVD events by 32%. The active treatment regimens were generally free of major adverse effects.

Similarly, the Systolic Hypertension in Europe (Syst-Eur) trial randomized 4695 persons aged 60 years and older with ISH (mean SBP 174 mmHg) to active treatment with nitrendipine with enalapril and hydrochlorothiazide added if necessary for BP lowering or placebo.[7] Syst-Eur was stopped after two years of follow up because it had reached the primary endpoint of a significant benefit (42% reduction) for stroke in the active treatment group. Mean SBP was 10 mmHg lower in the active treatment group at that time. All fatal and nonfatal CVD endpoints decreased significantly (33% reduction) with active treatment, but mortality was not affected, perhaps because of the abbreviated follow up period.

The Hypertension in the Very Elderly Trial (HYVET) randomized 3845 persons aged 80 years or older with a

mean baseline SBP of 173 mmHg to either active therapy with indapamide ± perindopril or placebo with a treatment target of SBP < 150 mmHg.[8] HYVET was terminated early (median follow up of 1.8 years) due to a significant (21%) reduction in total mortality in the active treatment group. Active treatment was also associated with a 30% reduction in stroke and a 64% reduction in heart failure. Significantly fewer serious adverse events were reported in the active treatment group.

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), the largest randomized controlled trial of BP lowering treatment ever conducted, provides an evidence base for choosing those antihypertensive agents that are most effective in preventing CVD events.[9] ALLHAT tested whether treatment with the dihydropyridine calcium channel blocker amlodipine or the angiotensin-converting enzyme inhibitor (ACEI) lisinopril lowers the incidence of coronary heart disease or other CVD events more effectively than treatment with the thiazide type diuretic chlorthalidone. ALLHAT randomized 33,357 persons aged 55 years or older (mean age 67 years) with hypertension and at least one other coronary disease risk factor to one of those three treatments. After a mean follow up of five years, the primary outcome, combined fatal coronary heart disease or nonfatal myocardial infarction and all-cause mortality, did not differ between treatment groups. The ALLHAT investigators concluded that thiazide-type diuretics are superior in preventing CVD and are less costly, and therefore should be preferred for first-step antihypertensive therapy. Following publication of the ALLHAT results, inexpensive generic calcium channel blockers and ACEI /angiotensin receptor blockers became available, and all four drug classes are recommended by current guidelines as first-step therapy for elderly hypertensive persons. These agents have also been used in subsequent NIH-funded outcome trials of antihypertensive therapy, such as Systolic Blood Pressure Intervention Trial (SPRINT).

The SPRINT tested the novel hypothesis that treating to a lower SBP target (< 120 mmHg) would reduce clinical events more than treating to the standard target of < 140 mmHg.[10] SPRINT randomized 9361 community-dwelling people with hypertension, average age 68 years, including 2636 ≥ 75 years of age (SPRINT-Senior). The average age of SPRINT-Senior participants was 80 years. The SPRINT intervention was stopped early for benefit. The intensive treatment regimen resulted in a 25% lower rate of the primary endpoint a composite of fatal and nonfatal major CVD events (myocardial infarction, other acute coronary syndrome, stroke, heart failure or death from cardiovascular causes), and a 27% lower rate of all-cause mortality compared to the standard intervention. There was also a 38% reduction in relative risk of heart failure and a 43% reduction in relative risk of death from cardiovascular causes in the intensive-treatment group. The benefits of intensive treatment were consistent in all pre-specified subgroups, including participants ≥ 75 years of age and were even slightly greater (33% reduction in the primary endpoint and 32% reduction in total mortality) in the senior group than in the study as a whole.

Secondary outcomes in SPRINT include decline in kidney and brain function, conditions that are of major concern for the aging hypertensive population. Main cognitive outcomes, including incident dementia, decline in cognitive function, and small-vessel cerebral ischemic disease assessed by MRI imaging, are currently being evaluated. Total serious adverse events did not differ between treatment groups, but conditions of interest classified as related to the intervention, including hypotension, electrolyte abnormalities, syncope, and acute kidney injury/acute renal failure were uncommon, but more frequent in the intensive-treatment group. Importantly, injurious falls were not more common and orthostatic hypotension assessed at clinic visits was significantly less common in the intensive-treatment group than in the standard treatment group. The pattern of adverse events in participants ≥ 75 years of age was similar to that in the study as a whole. SPRINT extends the findings of previous clinical trials of BP treatment in the elderly by demonstrating that lowering BP to a target lower than generally recommended is safe and effective in preventing CVD events in this high risk population.

After implementation of lifestyle interventions, BP should generally be treated with pharmacologic therapy to levels tolerated by the patient and supported by current guideline goals (Table 1).[13] First line agents for initial therapy include thiazide-type diuretics, dihydropyridine calcium channel blockers, and ACEI or angiotensin II receptor blockers. Most patients with BP elevation greater than 20/10 mmHg above BP targets will require two medications to achieve their treatment goals. Fixed dose combination therapy can help improve adherence and reduce medication burden. Beta-blockers, while beneficial for heart failure and prior myocardial infarction, have generally fallen out of favor as treatment for hypertension. Add on therapy with mineralocorticoid receptor antagonists or other medications that lower BP but have not been shown to prevent CVD events should be reserved for those who do not achieve BP control on first-line agents. Initiation of pharmacologic therapy should be followed with careful reassessment for adherence, side effects, and treatment responses.

Table 1. Guideline comparisons of goal BP and initial drug therapy for older adults with hypertension (adapted from reference [13]).

Guideline	Population	Goal BP, mmHg	Initial drug treatment options
2014 Hypertension guideline	General ≥ 60 yrs	< 150/90	Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB; Black: thiazide-type diuretic or CCB
	Diabetes	< 140/90	
	CKD	< 140/90	ACEI or ARB
ESH/ESC 2013	General elderly < 80 yrs	< 150/90	Diuretic, beta-blocker, CCB, ACEI or ARB
	General ≥ 80 yrs	< 150/90	
	Diabetes	< 140/85	ACEI or ARB
	CKD no proteinuria	< 140/90	ACEI or ARB
	CKD + proteinuria	< 130/90	ACEI or ARB
CHEP 2015	General < 80 yrs	< 140/90	Thiazide-type diuretic, ACEI (nonblack), or ARB
	General ≥ 80 yrs	< 150/90	
NICE 2011	General <80 yrs	< 140/90	CCB
	General ≥ 80 yrs	< 150/90	
ISHIB 2010	Black, lower risk	< 135/85	Diuretic or CCB
	Target organ damage or CVD risk	< 130/80	

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; CHEP: Canadian Hypertension Education Program; CKD: chronic kidney disease; CVD: cardiovascular disease; ESC: European Society of Cardiology; ESH: European Society of Hypertension; ISHIB: International Society for Hypertension in Blacks; NICE: National Inistitute for Health and Clinical Excellence.

2.3 Ongoing care and clinical implications of hypertension

Despite guidelines that support initiation and titration of antihypertensive therapy, only 54.1% of US adults achieve BP control.[3] The older adult is more likely to suffer from resistant hypertension, defined as BP that remains above goal in spite of concurrent use of three antihypertensive agents of different classes, ideally at optimal doses and including a diuretic, or requires 4 or more agents to achieve control.[14] The approach to BP that remains uncontrolled is to: (1) confirm the diagnosis with proper office or ambulatory measurements; (2) remove or reduce interfering substances such as excess dietary sodium and nonsteroidal anti-inflammatory drugs; (3) ensure adherence and try to use long-acting agents; (4) titrate medications to optimal doses using the preferred drug classes; and (5) evaluate for secondary causes of hypertension.[14]

Evaluation for secondary causes of hypertension should be considered for patients with resistant or accelerated hypertension. Hyperaldosteronism is the most common identifiable cause of resistant hypertension and can be screened with serum aldosterone and plasma renin activity measurements.[14] Utilization of aldosterone antagonists as add on therapy can be particularly useful in the treatment of resistant hypertension, but should include careful monitoring of potassium levels and renal function. Atherosclerotic renal vascular disease is more common in older than younger adults and should be suspected when BP accelerates suddenly. Results of randomized controlled trials of invasive treatment (stenting or surgical repair) of atherosclerotic renal artery stenosis have failed to show benefit on CVD outcomes.[15]

Finally, even adults with successfully treated hypertension remain at increased risk of CVD. Hypertension treatment should be part of a comprehensive approach to CVD risk reduction in older adults that includes smoking cessation, diagnosis and control of diabetes, treatment of dyslipidemia, lifestyle modification, and appropriate utilization of statin therapy.

3 Stroke

3.1 Diagnosis and evaluation

For many older adults, stroke is the most feared outcome, even more so than death. Fortunately, risk factor modification strategies for hypertension, cholesterol, diabetes mellitus, and smoking cessation have contributed to a decline in stroke mortality over the last decades. From 2003 to 2013, stroke death rates declined more among individuals aged ≥ 65 years old (–54.1%; from 534.1 to 245.2 per 100,000) than among younger age groups.[3] Yet in the US, about 610,000 people experience a first stroke and 185,000 a recurrent stroke each year, such that stroke causes about 1 in 20 deaths.

The majority of ischemic stroke events are due to atherosclerotic mechanisms that produce large artery occlusive disease or small vessel lacunar stroke. Therefore, aggressive risk factor modification and guideline-based therapy for hypertension, cholesterol, diabetes mellitus, and tobacco cessation are paramount to prevention.[16] Since embolic stroke from carotid stenosis is responsible for a significant proportion of these events and the prevalence of asymptomatic-greater-than-50-percent carotid stenosis in adults older than 65 years is 5%–10%, screening carotid Doppler studies should be considered in those with a high pre-test probability of disease. Additionally, in the older adult there is increased prevalence of atrial fibrillation, left ventricular dysfunction, valvular disease, and aortic arch atheroma, whereby rhythm monitoring and cardiac imaging impact treatment decisions.

3.2 Treatment

Guideline based therapy for stroke prevention depends upon the underlying etiology.[16] In older patients with nonvalvular atrial fibrillation, chronic anticoagulation therapy lowers the risk for embolic stroke by about two-thirds. Additionally, when stroke evaluation reveals a thrombotic source, anticoagulation is advised. Patients with carotid stenosis or other atherosclerotic etiologies should receive antiplatelet therapy, BP control, intensive statin therapy, glucose control, smoking cessation, lifestyle interventions and regular follow up.

Interventional therapy for extracranial carotid artery stenosis in the older adult is guided by a number of factors that should be weighed in the risk-benefit equation. These include patient age and expected longevity; symptom status; validated lesion severity; potential adherence to pharmacologic therapy; cerebral anatomy and function; vascular anatomic risk factors for stenting or endarterectomy; and experience, skill, and documented outcomes of the interventionalist or surgeon.

Symptom status is a critical first factor to consider. For patients with definite focal neurological symptoms (transient ischemia or stroke) that relate to a moderate to severe ipsilateral carotid stenosis, the risk of subsequent disabling stroke is high and significantly reduced by lesion treatment with carotid revascularization.[17,18] If stenting is the preferred choice of revascularization and the patient has a large (>1 cm) defect, the risk of cerebral hemorrhage will be reduced if the stenting procedure is delayed for two weeks. If surgery is the revascularization method of choice, then endarterectomy may be initiated sooner.

For asymptomatic patients with significant stenosis, current recommendations are controversial and are the subject of the National Institute of Neurologic Disorders and Stroke sponsored Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)2 trial. The basis for this study is that optimal and compliant pharmacologic and risk factor interventions have clinical equipoise with revascularization. The key terms are "optimal and compliant." Both terms are important considerations in deciding therapeutic options in the older adult. In CREST2, medical therapy without revascularization is considered the experimental arm since the CREST trial established a very low annual stroke risk (0.4%) after revascularization.[18] Given the relationship between stenosis severity and stroke risk, asymptomatic older adults should only be considered for revascularization if they have a severe degree of stenosis (> 70%–80%) validated by conclusive and accurate imaging modalities. Duplex velocity measurements should be complemented by additional high quality imaging, including angiography.

Peri-procedural risk of stroke is the major concern in older adults undergoing revascularization. Risk of peri-procedural minor stroke increases with age for both endarterectomy and stenting, but more so for patients > 75 years treated with stenting. This risk is mitigated in well selected older adults where less invasive percutaneous options may still have advantages in avoidance of operative and anesthetic complications (Table 2).[19–21]

Patient selection for carotid surgical endarterectomy in the older adult is also of critical importance. The CREST trial documented a significant increased risk of myocardial infarction with endarterectomy compared to stenting.[19] Further, the incidence of peri-procedural myocardial infarction was significantly associated with decreased survival after surgery. Other comorbid conditions (congestive heart failure, pulmonary and renal impairment) and anatomical issues (prior neck surgery, radiation and neck immobility) also significantly increase the risk of surgery. In older patients with risk factors for both stenting and endarterectomy, prudent intensive medical therapy is a good option.

Table 2. Patient selection: factors precluding carotid stenting in the older adult.

Decreased "cerebral reserve"
Prior large stroke
Dementia
Significant white matter disease
Diffuse intracranial atherosclerosis
Unfavorable vascular or lesion anatomy
Type 3 or vasculopathic aortic arch
Great vessel or internal carotid artery tortuosity
Moderate or heavy lesion calcification
Long, non-contiguous or complex lesion anatomy

4 Clinical pearls

(1) Hypertension is nearly ubiquitous in older adults, with isolated systolic hypertension being the most common form. (2) Correct measurement of blood pressure in the older adult is important for the diagnosis of hypertension and should be performed in both arms with correct positioning and appropriate equipment. (3) Treatment targets for older adults should be guided by tolerance of medications but generally benefit is seen when blood pressure is treated to the same levels as in younger populations. (4) First-line therapy for older adults should include thiazide-type diuretics, ACEI or angiotensin II receptor blockers, and/or dihydropyridine calcium channel blockers based on comorbid conditions and blood pressure levels. Beta-blockers, while beneficial for heart failure and prior myocardial infarction, have generally fallen out of favor. Add on therapy with mineralocorticoid receptor antagonists and agents from other classes that have not been shown in randomized trials to prevent CVD events should be reserved for those who do not achieve blood pressure control on first-line agents. (5) Management of hypertension in older adults should include lifestyle modifications, removal of interfering substances, and, when resistant or accelerated, consideration of secondary causes including hyperaldosteronism. (6) Most adults will require multiple agents, and attention to medication interactions and side effects is critical in the older adult. (7) Guideline based therapy for secondary stroke prevention depends upon the underlying etiology and includes blood pressure control, statin therapy, anticoagulation or antiplatelet therapy, smoking cessation and regular follow up. (8) In considering revascularization options for carotid disease (stenting versus endarterectomy), individual patient short-term as well as long-term risks should be weighed. Aggressive medical management may be the best strategy for older adults who are not revascularization candidates.

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