

REVIEW

Hypertension management in older adults [version 1; peer

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Abstract

Vascular aging leads to arterial hypertension, which is the leading cause of cardiovascular mortality and morbidity in older adults. Blood pressure reduction is effective in reducing the cardiovascular risk and is safe in ambulatory older adults. It is important to note that blood pressure control in this group of patients is challenging because of comorbidities, polypharmacy, and frailty. Choice of pharmacotherapy is not simple and should be individualized.

Keywords

hypertension, elderly, blood pressure

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What are the burden and mechanism of hypertension in older adults?

Vascular aging involves endothelial dysfunction and vascular remodeling. This process leads to an increase in large artery stiffness and isolated systolic hypertension, the predominant form of hypertension in older adults^{1,2}, affecting more than 75% of people older than 75 years in the US².

Hypertension is not a benign age-related phenomenon and indeed remains the leading cause of preventable cardiovascular mortality and morbidity³⁻⁶. The number of older patients continues to increase dramatically to be 8.5% of the world's current population and this percentage is expected to reach about 17% by 2050^7 . Hence, appropriate management of hypertension in this vulnerable population is crucial.

Do older adults benefit from blood pressure reduction?

Several randomized controlled trials have demonstrated that blood pressure (BP) lowering in systolic hypertension at an older age is effective in reducing the risk of fatal and non-fatal stroke, cardiovascular events, and death^{8–16}.

One of the few interventions shown to reduce mortality risk in older individuals is BP reduction. One of the earlier hypertension trials in this group of individuals was the Hypertension in the Very Elderly Trial (HYVET). Individuals older than 80 years with an initial systolic BP (SBP) greater than 160 mm Hg were assigned to receive either treatment or placebo10. Reduction of BP significantly decreased the incidence of fatal stroke, all-cause mortality, any cardiovascular event, and heart failure. Another important study that included older individuals was the Systolic Blood Pressure Intervention Trial (SPRINT). Patients older than 50 years with SBP greater than 130 mm Hg and at least one additional cardiovascular risk factor (presence of clinical or subclinical cardiovascular disease other than stroke, chronic kidney disease, a Framingham Risk Score for 10-year cardiovascular disease risk of at least 15, or age greater than 75 years) were enrolled. Patients were randomly assigned to intensive SBP lowering (<120 mm Hg) or routine SBP management (<140 mm Hg). The trial was concluded early because of overwhelming evidence of benefit. There was significant reduction of the primary outcome (myocardial infarction, acute coronary syndrome, stroke, congestive heart failure, or cardiovascular death) (5.2% versus 6.8%, hazard ratio [HR] 0.75, 95% confidence interval [CI] 0.64–0.89; P <0.0001). Among patients at least 75 years of age (n = 2,636), primary outcomes for intensive versus routine BP management were 7.7% versus 11.2% (P <0.05). Rates of all-cause mortality were 5.5% versus 8.1%, respectively (P <0.05). There was a significantly increased risk of hypotensive events and metabolic derangements such as hyponatremia with intensive treatment. It is important to note that generalizability of results was limited as patients with diabetes mellitus, history of stroke, and heart failure within 6 months and residents of nursing homes were excluded and less than 40% of patients were female¹⁷. The SPRINT trial not only showed the clear benefit of hypertension treatment at an older age but also brought a new perspective to the intensive BP control controversy in this vulnerable population.

Another relevant clinical question when it comes to treating hypertension in older individuals is whether it is beneficial for cognitive function. Longitudinal observational data have shown a strong association between elevated BP and cognitive decline later in life¹⁸; indeed, midlife hypertension is considered to be a major risk factor for dementia¹⁹.

Whereas several trials demonstrated a lower incidence of dementia with anti-hypertensive treatment in older individuals^{9,20-22}, others failed to show benefit and this was due in part to inadequate duration for follow-up²³⁻²⁵. A recently published substudy of the SPRINT trial (SPRINT-MIND) did not show a significantly reduced risk of probable dementia with intensive BP control²⁶. The study was terminated early and thus the cases of dementia were fewer than expected, and the study may have been underpowered for this endpoint. However, intensive BP control did significantly reduce the risk of mild cognitive impairment (14.6 versus 18.3 cases per 1000 personyears; HR 0.81, 95% CI 0.69–0.95) and the combined rate of mild cognitive impairment or probable dementia (20.2 versus 24.1 cases per 1000 person-years; HR 0.85, 95% CI 0.74– 0.97), which were predefined secondary endpoints.

What is the optimal target blood pressure in older adults?

Although the benefit of hypertension treatment in older adults has been clearly demonstrated, several cross-sectional studies have raised questions about the risk of hypotension and related cerebrovascular accidents, falls, and kidney failure^{27,28}; thus, the safety of BP reduction at an older age has been a controversial topic.

Recent US guidelines recommended initiation of antihypertensive drug therapy in older individuals with a BP greater than 130/80 mm Hg²⁰, although the BP target for treatment differed in European guidelines³⁰. This recommendation was based on several anti-hypertensive therapy trials that included large numbers of older individuals^{31–34}. Some patients with mild frailty were also included but most of these patients were ambulatory and able to travel to a clinic. In these trials, cardiovascular morbidity and mortality were reduced during BP lowering with different BP targets, including when the SBP treatment goal was less than 120 mm Hg. However, the risk of adverse outcomes, including orthostatic hypotension or falls, did not increase^{9,10,12,35}. Both HYVET and SPRINT included patients who were frail but still living independently in the community, and both were stopped early for benefit.

Thus, it is fair to say that BP control in ambulatory older patients seems to be safe. However, it is important to recognize that evidence-based recommendations for BP management are lacking in those who are very frail or institutionalized or those with cognitive impairment, several comorbidities, or polypharmacy. There is no evidence in the latter group that antihypertensive treatment reduces cardiovascular events or promotes established cognitive dysfunction³⁶, and evidence suggests that such treatment may not be safe³⁷. These individuals might be at risk for adverse consequences; thus, it is important for the clinician to pursue an individualized approach. Clinicians should carefully titrate BP lowering in persons with a high comorbidity burden^{37–39}.

Another important consideration is initiation of anti-hypertensive therapy with two agents. These individuals need to be monitored carefully for orthostatic hypotension and history of falls. BP must be measured both sitting and standing. Older persons may present with neurogenic orthostatic hypotension. This is particularly common in neurodegenerative disorders such as Parkinson's disease and hence should be taken into consideration.

What are the pharmacologic options for hypertension management in older adults?

Lifestyle measures are important in addition to pharmacotherapy. These include sodium restriction—Dietary Approaches to Stop Hypertension (DASH) diet—and physical activity⁴⁰. BP control in older adults is challenging because of the presence of other comorbidities, polypharmacy, and frailty. Physicians should individualize management to weigh the benefits and potential harmful effects of such therapy.

Common anti-hypertensive drugs, including diuretics, angiotensinconverting enzyme (ACE) inhibitors, calcium channel blockers, and even beta-blockers, have been shown to be effective in older adults^{41–44}.

It is important to note that each commonly used drug class has additional benefit in the presence of different comorbidities, such as ACE inhibitors in diabetes mellitus and beta-blockers in coronary disease. Decisions should be based on efficacy, tolerability, cost-effectiveness of each drug, and the presence of specific comorbidities and polypharmacy and thus drug interactions.

Beta-blockers should be used cautiously in older patients as these individuals are particularly sensitive to bradycardic effects. The main adverse effects of calcium channel blockers are related to edema and orthostatic hypotension. Also, constipation might be a significant limitation with diltiazem and verapamil. Nitrates are useful during hypertensive emergencies and angina; however, they are not preferred for long-term BP control at an older age. Owing to their side effect profile, peripheral agents such as hydralazine and minoxidil are not first-line agents. A centrally acting agent, clonidine, can be used for BP management. Owing to reflex hypertension when discontinued, oral clonidine is not advised; clonidine patch averts this problem. It has several side effects, including bradycardia and sedation, both of which are problematic in older and frail individuals. Diuretics should be used with caution as urinary incontinence can be a major concern in older adults.

Another important consideration in the management of hypertension in older individuals is to use ambulatory BP monitoring instead of relying on single office measurements. The development of isolated systolic hypertension (and thus wide pulse pressure), white coat effect, different measurements between ambulatory and clinical BP, prevalence of orthostatic hypotension, and medication interactions are among the reasons that necessitate ambulatory BP monitoring⁴⁵.

Finally, another important consideration is de-escalation of anti-hypertensive medications in patients who are intolerant. The Discontinuation of Anti-hypertensive Treatment in Elderly people (DANTE) study showed that in older individuals with orthostatic hypotension, discontinuation of anti-hypertensives showed significant recovery from orthostasis⁴⁶. Discontinuation of therapy might also be considered in older patients approaching the end of life, in whom the burden of therapy might exceed the purported benefit.

What are the future considerations?

Randomized clinical trials are needed in frail older individuals with hypertension residing in nursing homes to determine both the benefits and adverse effects of anti-hypertensive drug therapy in this vulnerable population.

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