



Hypertension and Its Treatment in the Elderly



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Received:  December 24, 2018; **Published:**  January 16, 2019

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Mini Review

The treatment of hypertension has been shown to be accompanied by a reduction in mortality and morbidity both in older and younger hypertensive patients. In the elderly hypertensive patients BP should be lowered to a systolic value of 130-139 mmHg and a diastolic value of <80 mmHg if tolerated. Treated SBP values of <130 mmHg should be avoided and in the elderly hypertensive patients it should be advised to undertake treatment together with an evaluation of the presence of other comorbidities and the risks associated with multi-therapy, especially in the older. Hypertension is a known risk factor for cardiovascular morbidity and mortality and in the long term one of the main causes of end stage renal disease. The definition of hypertension does not change with age: office blood pressure value at least 140 mmHg for systolic blood pressure (SBP) and diastolic blood pressure (DBP) at least 90 mmHg is defined as grade 1 hypertension [1].

Although rise in blood pressure is not a normal part of aging, the incidence of hypertension in the elderly population is high. In the 1988-2004 National Health and Nutrition Examination Survey 67% of adults aged 60 and older were found to be hypertensive [2]. Data from the Framingham study show that 58.9% of people aged ≥65 and 70% of those aged ≥80 years are hypertensive [3]. SBP rises progressively until the age of 70 or 80, whereas DBP increases until the age of 50 or 60 and then tends to level or even decline slightly. This combination of changes likely reflects aged related increase in stiffness of the blood vessels [4]. Arterial compliance is reduced by wall thickening, calcium accumulation, quantitative and qualitative alterations in collagen [5]. Baroreceptors sensitivity is altered with age and this may explain the variability of blood pressure revealed by continuous monitoring [6]. Vascular oxidative stress increases with aging, leading to pro-inflammatory phenotypical changes and an altered endogenous bioavailability of vasoactive substances with consequent impaired vascular function

and changes in smooth muscle tone; this leads to an impairment of postural reflexes, making elderly hypertensive individuals more sensitive to orthostatic hypotension [7].

The loss of diastolic augmentation caused by the stiffness of major arteries leads to a fall in perfusion pressure in the coronary arteries, and changes in cerebrovascular circulation lead to reductions in cerebral perfusion [8]. Renal perfusion decreases with aging and determine an impairment of renal function with and reduction of the glomerular filtration rate [9]. All these changes could explain the decreased cardiac output, decreased heart rate, decreased myocardial contractility, nephroangiosclerosis, left ventricular hypertrophy seen in elderly patients and increased cardiovascular risk respect to general population. The cardiocerebrovascular-renal risk from hypertension is demonstrated by the higher incidence of stroke, left ventricular hypertrophy, congestive heart failure, coronary and peripheral artery diseases, vision impairment, end-stage renal disease, cognitive impairment, and dementia seen in the elderly hypertensive patients [10]. A large amount of evidences demonstrates that lowering blood pressure can substantially reduce this high morbidity and mortality [11-13].

“To be, or not to be, that is the question” in this way Hamlet asked himself if should be better to act against his enemies or get loose. In the same way we can ask ourselves to “treat (and how) or not treat” the hypertension of the elderly patient. Treatment of hypertension in the elderly is a hotly debated topic because this type of patient has an increased risk of cardiovascular disease, chronic kidney insufficiency and dementia. On the other side it is essential to consider the possible side effects that antihypertensive therapy can cause in the elderly subject: orthostatic hypotension, acceleration of cognitive decline, reduction of coronary perfusion with consequent myocardial ischemia. In the SPRINT trial, in fact, a significant reduction in the risk of cardiovascular events in elderly

patients is associated with an increase in renal damage and syncope episodes [14,15].

The current guidelines, although advising to treat patients over 65 years who have hypertension, are not aligned on which systolic blood pressure and diastolic blood pressure values a treatment can be started. The members of the US Eighth Joint National Committee recommended in 2014 that in older individuals, antihypertensive treatment should be initiated at SBP values above 150 mmHg and SBP reduced to values lower than 150 mmHg [16]. The 2017 High Blood Pressure Clinical Practice Guideline of the American Heart Association/American College of Cardiology makes a strong recommendation (Level of Evidence A) to initiate antihypertensive drug treatment in individuals of 65 years or older with SBP of 130 mmHg or higher with a treatment goal of less than 130 mmHg [17]. The European Society of Cardiology and the European Society of Hypertension 2018 guidelines recommend that in older patients treated for hypertension, blood pressure should be lowered to <140/80 mmHg, but not below 130mmHg for SBP.

SBP target range of 130–139 mmHg is recommended for people older than 80 years, if tolerated. Blood pressure lowering drug treatment and lifestyle intervention is recommended in fit older patients (>65 years but not >80 years) when SBP is in the grade 1 range (140–159 mmHg), provided that treatment is well tolerated. In all patients is recommended to initiate an antihypertensive treatment with a two drugs combination, preferably in a single pill combination. The exceptions are frail older patients and those at low risk and with grade 1 hypertension (particularly if SBP is <150 mmHg). SBP thresholds suggested for initiating treatment are ≥ 140 mmHg in patients aged 65–79 and ≥ 160 mmHg in patients aged ≥ 80 ; DBP threshold for treatment is ≥ 90 mmHg in both patient groups aged 65–79 and ≥ 80 . The impact of blood pressure-lowering on the well-being of the patient should be closely monitored, because the increased risk of adverse events (e.g. injurious falls) with lower blood pressure values could be more pronounced in older patients in the real-life setting than in the closely monitored conditions of randomized controlled trials. Recommended initial therapy, for all ages, for uncomplicated hypertension, is one pill with dual combination of ACE inhibitor (ACEi)/angiotensin renin blocker (ARB) + calcium channel blocker (CCB)/diuretic. Second step therapy is one pill with a triple combination of ACEi /ARB + CCB + diuretic.

Third step therapy, for resistant hypertension, is 2 pills with triple combination of above + spironolactone or other diuretic, alpha-blocker or beta-blocker. Consider beta-blockers at any treatment step, when there is a specific indication for their use (e.g. heart failure, angina, post-myocardial infarction, atrial fibrillation). Drug initial treatment strategy, for any age, for hypertension and coronary artery disease, is a triple combination of ACEi/ARB + beta-blocker/CCB or CCB + diuretic/beta-blocker or beta-blocker + diuretic. Second step therapy is one pill with a triple combination

of above considering initiating therapy when SBP is 130 mmHg in these very high-risk patients with established cardiovascular disease. Third step therapy, for resistant hypertension, is 2 pills with triple combination of above + spironolactone or other diuretic, alpha-blocker or beta-blocker. Drug treatment strategy for hypertension and chronic kidney disease, for all ages, is one pill with dual combination of ACEi /ARB + CCB or ACEi /ARB + diuretic (use loop diuretics when eGFR is <30 mL/min/1.72 m²).

Second step therapy is one pill with a triple combination of ACEi/ARB + CCB + diuretic (use loop diuretics when eGFR is <30 mL/min/1.72 m²). Third step therapy, for resistant hypertension, is 2 pills with triple combination of above + spironolactone or other diuretic, alpha-blocker or beta-blocker. A reduction in eGFR and rise in serum creatinine is expected in patients with chronic kidney disease who receive blood pressure therapy especially in those treated with ACEi or ARB [1]. Are there any benefits in treating the elderly patient with antihypertensive therapy and at what values of SBP and DBP is it possible to start a treatment? For many years, advanced age has been a barrier to the treatment of hypertension due to concerns about potential poor tolerability. This approach does not seem appropriate, because evidence from randomized controlled trials has shown that in old and very old patients, antihypertensive treatment substantially reduces cardiovascular morbidity and cardiovascular and all-cause mortality [18]. A recently published meta-analysis by Thomopoulos et al. has identified and analyzed 32 blood pressure-lowering randomized controlled trials with data on 95,549 older patients and 31 randomized controlled trials on 114,009 younger patients. Significant reductions in the relative risk of all major mortality and morbidity outcomes were observed in elderly and young patients without significant differences. Moreover, a reduction of systolic blood pressure between 140 and 150 mmHg in older patients significantly reduces the risk of stroke and major cardiovascular events.

Fatal and nonfatal stroke, fatal and nonfatal coronary heart disease events, fatal and nonfatal hospitalized heart failure, composite of stroke and hospitalized heart failure, cardiovascular death were considered outcomes of mortality and morbidity. Furthermore, no significant differences were found using as a cut-off of 60 or 65 years, and patients treated up to 80 years have shown a significant reduction of stroke, heart failure and major cardiovascular events. The meta-analysis also suggested that it is possible to initiate antihypertensive treatment in individuals over 60 with an untreated baseline systolic blood pressure of 140–149 mmHg although there are not many clinical trials in elderly patients. This study also shows that the prudent recommendation of not depriving older hypertensive patients with grade 1 systolic blood pressure elevation (systolic 140–159 mmHg and/or diastolic 90/99 mmHg) of the possible benefits of treatment is not only founded on experts opinion but is supported by evidence at least when an

age cut-off of 60 years is used [19]. Regarding the treatment of diastolic hypertension, it is essential to consider the risk of organ hypoperfusion (particularly myocardium) in the elderly patient, who usually has already reduced diastolic blood pressure values.

It is recommended to maintain a diastolic blood pressure target between 70 and 79 mmHg, paying attention to the risk of organ hypoperfusion. The results of Thomopoulos' meta-analysis could be compared with the 2008 Blood Pressure Lowering Treatment Trialists Collaboration meta-analysis that did not find significant differences between the effects of BP-lowering treatment in older and younger individuals [20]. It would be useful to create a score that groups frailty syndrome in the elderly to the major patients' comorbidities (renal failure, cognitive impairment, risk of falls and fractures, cardiovascular risk) to identify a score beyond which the introduction of antihypertensive therapy is recommended and useful, as for example, Fried et al have done for the definition of frailty: a clinical syndrome characterized by three or more of the following: unintentional weight loss of 10 lbs or more in the past year, self-reported exhaustion, weakness measured by grip strength, slow walking speed, and low physical activity is a good example [21].

Conclusion

The treatment of hypertension has been shown to be accompanied by a reduction in mortality and morbidity both in older and younger hypertensive patients. In the elderly hypertensive patients, it should be advised to undertake a hypertensive treatment together with an evaluation of the presence of other comorbidities and the risks associated with multi-therapy, especially in the older. BP should be lowered to a systolic value of 130–139 mmHg and a diastolic value of <80 mmHg if tolerated. Treated SBP values of <130 mmHg should be avoided. It is essential to underline that the elderly patient is a difficult patient to treat and therefore deserves a "sartorial therapy" with a careful evaluation of the risks and benefits. Clinicians can successfully respond to the Hamlet question and choose an adequate antihypertensive therapy for older patients. The introduction of a score that groups frailty syndrome in the elderly to the major patients' comorbidities could help to dissolve doubts.

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ISSN: 2574-1241

DOI: [10.26717/BJSTR.2019.13.002358](https://doi.org/10.26717/BJSTR.2019.13.002358)

Lorenzo A C. Biomed J Sci & Tech Res



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