Effective Hypertension in older adults with chronic kidney disease. Many missing links?

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• More than 60% patients of chronic kidney diseases (CKD) have hypertension. Control of blood pressure (BP) in CKD subjects is an important strategy to reduce the burden of cardiovascular disease, the progression of CKD, development of end-stage renal disease (ESRD), and mortality.
Chronic Kidney Disease

- Cardiovascular disease
- Osteoporosis
- Hypertension
- Diabetes Mellitus
- Ageing
• From **30 to 40 years of age**, the GFR generally (but not invariably) declines.

• In the older person, tubular and endocrine dysfunction in the kidney are common.


• Showed that 37.8% of subjects >70 years had a GFR of <60 ml/min/1.73 m², this prevalence had increased from 27.8% in the NHANES 1988–1994 data.


With greater access to health care among the elderly, this group is the fastest-growing population requiring dialysis, with 25% and 21.3% of dialysis patients in the United States and Australia, respectively, being ≥75 years of age and between 31 and 36% of patients receiving renal replacement therapy in different regions of the United Kingdom being >65 years of age.
Among NHANES III (1988–1994) subjects aged ≥60 years of age, either treated or not treated for a high BP, there was a J-shaped relationship between BP and CKD prevalence. Thus, persons with a systolic BP of 120 to 159 mm Hg or a diastolic BP of 80 to 99 mm Hg had the lowest CKD prevalence, with a higher prevalence associated with a systolic BP <120 mm Hg or diastolic BP <80 mm Hg and a systolic BP ≥160 mm Hg or a diastolic BP ≥100 mm Hg.
Analyses of data NHANES, indicate that with increasing age, there is an increase in the prevalence and severity of CKD, confirming the strong relationship between BP and CKD in the elderly.


• The elderly patients has thus been focused more on systolic than diastolic BP

SHEP study
• In an analysis of 2181 persons >65 years of age in the placebo arm of this study, systolic BP was more predictive of decline in kidney function

CKD in the elderly

- Arteriolar sclerosis, global glomerulosclerosis, and tubular atrophy are more common in the elderly.
- Although selection bias is likely, a kidney biopsy series of 413 patients aged 66 to 79 years and 100 patients aged 80 to 89 years showed nephrosclerosis in 34% of patients >80 years and in 7% of those 66 to 79 years.

Renal vascular disease in the elderly. Gómez Campderá FJ, Luño J, García de Vinuesa S, Valderrábano F

Renal biopsy in patients aged 80 years and older. Nair R, Bell JM, Walker PD
Macrovascular disease is particularly common. This might influence BP targets or the preferred agents use to control BP, especially if heart failure, angina, cerebral vascular insufficiency, or peripheral vascular diseases are prominent.
Hypertension is a global health problem that contributes significantly to the cardiovascular and kidney disease morbidity and mortality of our aging population. In this context, it is clear that BP increases not only as we age but also as kidney function starts to decline.
A series of retrospective analyses of INVEST has further highlighted the issue of J-shaped relationships between systolic BP, diastolic BP and outcomes in elderly hypertensive patients with Coronary Artery Disease.


Blood pressure and outcomes in very old hypertensive coronary artery disease patients: an INVEST substudy. Denardo SJ, Gong Y, Nichols WW, Messerli FH, Bavry AA, Cooper-DeHoff RM, Handberg EM, Champion A, Pepine CJ

Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary artery disease. Cooper-DeHoff RM, Gong Y, Handberg EM, Bavry AA, Denardo SJ, Bakris GL, Pepine CJ
The risk of all cause mortality and myocardial infarction, but not stroke, increased with reductions in diastolic BP in the patient group as a whole, all of whom had coronary artery disease and were being treated for high BP.

In patients aged 70 to 80 years, risk increased once systolic BP was less than 135 mm Hg or diastolic BP <75 mm Hg, while the risk increasing when systolic BP was <140 mm Hg or diastolic BP <70 mm Hg in patients ≥80 yrs.

• The Hypertension in the Very Elderly Trial (HYVET), involving patients 80 years of age or older, provided further assurance that BP lowering treatment of very elderly patients with a sustained BP of ≥160 mm Hg is beneficial.


Thus BP targets in the elderly, with or without CKD, should be set only after consideration of co-morbidities and should be achieved gradually. Based on the evidence on BP in the elderly (not selected for CKD), recent guidelines and consensus documents generally agree that <140/90 mm Hg should be the target in uncomplicated hypertension.
• A reasonable approach might be to use BP targets as recommended in the younger CKD population (≤140/90 mm Hg in non-albuminuric CKD and ≤130/80 mm Hg in albuminuric CKD), but to reach these targets gradually, bearing in mind that they may not be achievable without adverse effects particularly in a patient with multiple age-related co-morbidities. It is even more difficult to make recommendations in patients over 80 years of age with CKD due to the lack of evidence.

The most recent report from the panel members appointed to the Eighth Joint National Committee recommend a BP target of $<150/90$ mmHg for all adults aged $\geq 60$ years and $<140/90$ mmHg for those aged $<60$ years.

In the context of the aging patient with CKD, recent observational studies questioned the utility of lowering systolic BP (SBP) <130 mm Hg for all patients irrespective of age.

_Blood pressure and mortality in U.S. veterans with chronic kidney disease: A cohort study._ Kovesdy CP, Bleyer AJ, Molnar MZ, Ma JZ, Sim JJ, Cushman WC, Quarles LD, Kalantar-Zadeh K

• The Kidney Disease Improving Global Outcomes (KDIGO) Blood Pressure in CKD work group recommends a target BP of ≤140/90 mmHg in those with CKD (both diabetic and nondiabetic) and urine albumin excretion <30 mg/24 h and suggests a target BP of ≤130/80 mmHg in those with CKD (both diabetic and nondiabetic) and urine albumin excretion >30 mg/24 h irrespective of age.
• The KDIGO guidelines did not recommend a specific BP target for elderly persons with nondialysis-dependent CKD because of a lack of conclusive evidence.
The cohort included 21,015 adults, aged 65–105 years, with an eGFR < 60 ml/min per 1.73 m² and hypertension defined using relevant International Classification of Diseases-9 codes, BP values obtained from the electronic health record, and antihypertensive therapy.
The authors modeled the relationship using multivariable Cox proportional hazards model that suggested among those aged 65–70 years, a U-shaped association was noted between SBP and death, with the highest hazards for those with SBP<130 and >140 mmHg. Among those aged >70 years, SBP<130 mmHg was associated with a higher risk for death, but SBP>140 mmHg was not associated with death.
• Data from a study of the Kidney Early Evaluation Program study suggest that the risk for CKD progression was higher among those with SBP=140 mmHg and highest among those with SBP≥150 mmHg.

Similarly, findings from the **Chronic Renal Insufficiency Cohort study** (prospective longitudinal study) using time-updated data show that SBP>130 mmHg was more strongly associated with CKD progression.


• Apart from age, *per se*, older adults with CKD suffer from electrolyte disorders, bone disease (metabolic bone disease and osteoporosis), and muscle atrophy predisposing them to falls and subsequent hospitalizations. There is significant concern for intense BP control and the risk for orthostatic hypotension and falls in this population.

The risk of falls on initiation of antihypertensive drugs in the elderly. Butt DA, Mamdani M, Austin PC, Tu K, Gomes T, Glazier RH. *Osteoporos Int* 2013; 24: 2649–2657.
• **Veterans Affairs cohort,** Kovesdy *et al.* reported that DBP of 80–90 mmHg is associated with better survival. Weiss *et al.* provide new information by noting that patients with DBP<60 mmHg and >80 mmHg had higher risk for death irrespective of age.
SBP>130–139 mmHg is associated with higher mortality and higher incidence of Coronary Heart Disease, stroke, and ESRD in patients with CKD of all ages, but the strength of these associations diminishes with advanced age. DBP<70 mmHg is associated with higher mortality, but DBP shows no association with cardiovascular outcomes.
The SPRINT study showed that treating SBP to a target of <120 mmHg (with an overall achieved SBP of 121.4 mmHg) versus <140 mmHg (with an achieved SBP of 136.2 mmHg) resulted in significantly lower all-cause mortality rate and nominally lower composite cardiovascular event rate in patients with CKD.


These results support our findings regarding the lower risk of Coronary Heart Disease and stroke associated with lower SBP but may be discordant with the J-shaped mortality seen in our and other observational studies, even though we have only detected statistically significantly higher mortality for patients with SBP<110 mmHg.
SPRINT enrollees had markedly lower all-cause mortality rates compared with the populations examined in observational studies, which may be experiencing relatively more deaths unrelated to cardiovascular events. It is unclear whether they would derive a mortality benefit from SBP lowering to levels even stricter than those achieved in SPRINT.
• The treatment of hypertension in younger patients with CKD toward targets recommended by current clinical guidelines is paramount to improve outcomes in these patients.

• In very elderly patients with CKD a more cautious BP-lowering strategy may be reasonable.
Thank you