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Stricter systolic blood pressure control is associated with higher all-cause mortality in patients with chronic kidney disease

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Context

Hypertension is a major cause of mortality. Previous studies have identified a J-shaped association between systolic blood pressure (SBP) and risk of mortality, raising concerns about the safe limits of blood pressure lowering in certain patient populations. Patients with chronic kidney disease (CKD) represent 13% of the US population and have high prevalence of cardiovascular morbidity and a high mortality rate. However, data on optimal blood pressure targets in this high-risk patient population is limited. The few published trials of blood pressure in patients with CKD have primarily focused on kidney end points.¹² Prior observational studies of patients with CKD have suggested that lower SBP is associated with higher risk of death.³

This study was performed to augment these prior studies. It was an observational study of US veterans with a CKD which examined risk of death associated with treated SBP of <120 (strict) versus 120–139 mm Hg (conventional).

Methods

This was a retrospective cohort study of US veterans with CKD with uncontrolled systolic hypertension. Uncontrolled systolic hypertension was defined as SBP ≥ 130 mm Hg and/or use of antihypertensive medications. All blood pressure measurements were obtained from clinical practice. Patients were followed until the primary outcome of all-cause mortality or end of study period. Median follow-up time was 6.0 years. To model therapeutic interventions resulting in improved blood pressure control, patients were categorised on the basis of SBP recorded during their follow-up visits, either achieving SBP <120 or 120–139 mm Hg on at least 50% of all follow-up visits. To account for possible bias caused by differences in baseline clinical characteristics in reference to subsequent SBP, propensity scores for the likelihood of SBP <120 vs 120–139 mm Hg were generated.

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Competing interests None.

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Findings

Overall 77 765 patients with CKD with uncontrolled systolic hypertension were included in the analysis. Of these patients, 5750 had follow-up treated SBP of <120 mm Hg and 72 005 patients had an SBP 120–139 mm Hg. The unadjusted HR of mortality with follow-up SBP <120 vs 120–139 mm Hg was 2.08 (95% CI 1.99 to 2.17), which was attenuated but remained significant after adjustment for propensity scores (HR 1.70 (95% CI 1.63 to 1.78)) and differences in baseline characteristics (HR 1.74 (1.65 to 1.83)) as well as in the propensity-matched cohort (HR 1.61 (1.51 to 1.71)). Results were consistent in subgroups by demographics, Charlson comorbidity index, estimated glomerular filtration rate, diabetes, coronary heart disease and chronic heart failure.

Commentary

This paper reinforces findings previously reported by this research group³ which suggests that lower SBP is associated with higher risk of all-cause mortality in CKD. The unique aspect of this paper is the ‘clinical trial modelling’ approach the authors applied to this observational study. The authors reason that this approach may complement clinical trials and may in fact study a more generalisable patient population compared with clinical trial participants. The findings presented in the analyses are sound and not surprising.

However, several limitations must be noted. This analysis relied on clinical SBP measures which may introduce some bias. Patients with either high or low SBP are likely to have SBP measured more frequently. It was not clear whether inpatient SBP measures were included. The authors were not able to account for interim illnesses/morbidity or hospitalisations that may have effected SBP level or treatment. We cannot determine whether the effect seen on risk of death was secondary to SBP level or class of antihypertensive used. The study population was primarily white older males and thus may not be generalisable to the overall CKD population. Finally, although the authors attempted to use an observational data set to perform ‘clinical trial modelling’ the results cannot be interpreted as those from a clinical trial—significant differences in patient characteristics were noted in the strict versus conventional arms. The use of propensity scores may not fully account for this bias, thus the issue of residual confounding is a concern.

Implications for practice

This study strengthens the body of observational literature suggesting that lower SBP may be associated with higher risk of adverse outcomes among patients with CKD. It also supports the need for future clinical trials among the high-risk CKD population to elucidate the optimal goals and treatment of SBP to decrease the risk of cardiovascular disease and death.

References

1. Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. *N Engl J Med.* 1994; 330:877–84. [PubMed: 8114857]

2. Wright JT Jr, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA. 2002; 288:2421–31. [PubMed: 12435255]
3. Kovesdy CP, Bleyer AJ, Molnar MZ, et al. Blood pressure and mortality in U.S. veterans with chronic kidney disease: a cohort study. Ann Intern Med. 2013; 159:233–42. [PubMed: 24026256]