Chapter 11: Hypertension, Chronic Kidney Disease, and the Elderly

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The major goals of lowering BP in patients with chronic kidney disease (CKD) include reduction of mortality, cardiovascular events, and slowing progression. Key considerations in the management of hypertension include selection of a target BP and selection of agents used to attain the chosen target. This chapter outlines key considerations in applying current guidelines for the management of BP to older patients with CKD.

BP TARGETS

Many clinical practice guidelines recommend a lower than usual BP target for patients with CKD. For example, the Kidney Disease Outcomes Quality Initiative (KDOQI) recommends a target BP of <130/80 mmHg for all patients with CKD, which is defined as an eGFR <60 ml/min per 1.73 m^2 or "kidney damage" (specified as microalbuminuria or macroalbuminuria for patients with diabetes). Citing KDOQI, the seventh report from the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) also recommends a target BP of <130/80 mmHg for all patients with CKD defined as an eGFR <60 ml/min per 1.73 m^2 or protein-to-creatinine ratio ≥200 mg/g.[1] A target BP <130/80 mmHg is also recommended by the American Diabetes Association (ADA) and by JNC 7 for all patients with diabetes.

Despite the consistency of guideline recommendations for lower than usual BP targets in patients with CKD, these recommendations are based on opinion rather than the results of randomized controlled trials. Few trials have shown that treatment to lower than usual BP targets slows progression of CKD or reduces other clinically significant outcomes in patients with CKD (Table 1). On the other hand, available evidence also suggests that treating to lower than usual BP targets is not associated with an increased risk of adverse outcomes.

BP TARGETS IN THE ELDERLY

In applying this recommendation to the elderly, it is worth noting that none of the trials used to support the safety of lower than usual BP targets in patients with CKD enrolled any participants older than 75 (Table 1). Thus, the safety of treating to a lower than usual BP level in older patients with CKD is not known. Indeed, in the very elderly (*e.g.,* 85 yr or older), observational data showed that there is a J-shaped relationship between BP and survival and that optimal BP may be higher than in younger people.[2,3] Although a number of trials have specifically examined the effect of BP lowering on nonrenal outcomes in the elderly, and in many instances have shown a benefit, these trials have tended to target a higher than usual (rather than lower than usual or even usual) BP.[2,4–7]

In pursuing a lower than usual BP target in an older person, it is important to assess the importance to that patient of the implicit goals of this intervention (*e.g.,* slowing progression of CKD and reducing cardiovascular risk) as well as the potential harms. For a variety of reasons, it is likely that for many patients who meet criteria for CKD, the risk-to-benefit ratio of BP lowering may differ from that in younger patients. First, CKD in the elderly is often slowly progressive or nonprogressive, and the risk of progression to end-stage kidney disease (ESKD) is lower for older than for younger patients

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Table 1. Trials examining the effect of blood pressure lowering on progression of CKD by diabetic status

	Blood Pressure Targets	Outcome	Subgroup or Secondary Analyses	Age Inclusion Criteria (yr)	Mean Age (yr)
Diabetes					
Estacio *et al.*[23] and Schrier *et al.*[24]	DBP < 75 *versus* 80–89	No difference in progression		40–74	59.5
Lewis *et al.*[25]	MAP < 92 *versus* 100–107	No difference in progression		18–40	37
UKPDS[26]	<150/85 *versus* <180/105	No difference in progression	Reduced risk of microalbuminuria at 6 yr	25–65	56
No diabetes					
Ruggenenti *et al.*[27]	DBP < 90 *versus* 130/80	No difference in progression		18–70	54
Wright *et al.*[28]	MAP 102–107 *versus* ≤92 (125/75)	No difference in progression	Trend toward greater benefit in patients with proteinuria	18–70	54.6
Klahr *et al.*[29]*	MAP ≤107 *versus* <92	No difference in progression	Secondary analysis showed greater benefit in patients with greater degrees of proteinuria	18–70	52

*The MDRD study had different blood pressure targets based on age and required a MAP ≤ 107 (equivalent to 140/90) for patients 18 to 60 yr of age and MAP ≤ 113 for patients ≥61 yr of age (equivalent to 160/90) or low blood pressure <92 (125/75) for patients 18 to 60 yr of age and MAP ≤ 98 mmHg (equivalent to 145/75) for patients ≥61 yr of age.
DBP, diastolic blood pressure; MAP, mean arterial pressure.

with similar levels of eGFR.[8,9] Thus, there may be less to be gained from slowing progression if this is slow to begin with. It is also not clear that mortality risk for most elderly patients with a low eGFR is any higher than for their age peers with a "normal" eGFR.[10,11] The majority of older patients who meet criteria for CKD have very moderate reductions in eGFR (*e.g.*, 45 to 59 ml/min per 1.73 m^2). For many of these patients, the relative and absolute risk of death may be no greater than for patients of the same age whose eGFR falls in the normal range.[10,11] Thus, it is not even clear that reducing mortality risk provides a compelling rationale for a lower than usual BP in many older patients with an eGFR <60 ml/min per 1.73 m^2. Second, it is not clear that slowing progression of CKD is always the most meaningful goal of anti-hypertensive therapy in older patients with a low eGFR.[9,12]Their risk for other outcomes such as cardiovascular events, disability, and cognitive insufficiency is often much higher than that for ESKD. CKD in the elderly rarely occurs in the absence of other comorbid conditions.[9,13] The presence of multiple comorbid conditions in older patients with CKD may complicate the management of CKD by creating potentially conflicting or competing treatment goals. Third, the potential harms of BP lowering may be greater in the elderly. Most elderly patients with CKD have isolated systolic hypertension. Thus, theoretically, treatment of their systolic hypertension may have the unintended effect of lowering diastolic pressure to suboptimal levels, leading to impaired perfusion during diastole. Orthostatic hypotension is also more common in the elderly and may be aggravated by treatment to lower than usual BP targets. Finally, elderly patients, particularly those who are frail, may be more likely to experience injury as a result of an episode of hypotension.

In summary, in deciding whether to target a lower than usual BP in older patients who meet criteria for CKD, the clinician must consider each individual patient's likelihood of experiencing progressive loss of renal function and mortality in relation to their age peers and in the context of their risk for other (perhaps competing) health outcomes and their risk for adverse events as a result of BP lowering.

CHOICE OF AGENTS

In addition to lowering BP, progression of CKD can probably also be slowed by reducing proteinuria.[14] For this reason, angiotensin-converting enzyme inhibitor (ACEI) and angiotensin II receptor antagonists (ARBs) are considered first-line agents for patients with CKD in a number of different clinical practice guidelines. KDOQI recommends that these agents be prescribed for patients with diabetic CKD (defined as an eGFR <60 ml/min per 1.73 m^2 or micro- or macroalbuminuria) and for those with nondiabetic proteinuric CKD, even in the absence of hypertension.[1,15,16] Based on recommendations from KDOQI and a subset of trials referenced in KDOQI, JNC 7 identifies CKD, defined as an eGFR <60 ml/min per 1.73 m^2 or a protein-to-creatinine ratio ≥200 mg/g, as a compelling indication for the use of ACEI or ARB.

CHOICE OF AGENTS IN THE ELDERLY

In applying these guidelines to the management of older patients with CKD, it is important to note that many of the key studies supporting these recommendations did not include participants older than 70.[17–19] Nevertheless, a subgroup analysis among participants older than 65 enrolled in the RENAAL trial, a trial among type II diabetics with macroalbuminuria,[20]

Losartan was similarly renoprotective in these older participants as it was in the overall study population, suggesting that this agent is equally efficacious in elderly patients with albuminuria. Like RENAAL, most trials of ACEI and ARB in patients with CKD that are cited in contemporary guidelines explicitly or implicitly selected for proteinuria. However, the trial that enrolled by far the largest number of older participants with CKD (the Antihypertensive and Lipid Lowering to Prevent Heart Attack or ALLHAT) did not select for proteinuria (because level of urinary protein was not ascertained at baseline or follow-up).[21] Participants in ALLHAT with an eGFR <60 ml/min per 1.73 m^2 had a mean age of 70.8 yr and had a similar risk of ESKD regardless of whether they received an ACEI, thiazide diuretic, or calcium channel blocker. This was true both overall and for the subset with diabetes. This study certainly raises the question of whether ACEI confer greater protection against renal outcomes in elderly patients with CKD unselected for proteinuria.

Furthermore, similar principles apply to choice of agent as apply to BP targets in the management of hypertension in elderly patients with a low eGFR. Use of ACEI and ARB is recommended for the management of hypertension in CKD based on the ability of these agents to slow progression, which for reasons outlined above, may not always represent the most patient-centric goal of therapy. In older patients who meet criteria for CKD, the goals of anti-hypertensive therapy in many instances should perhaps be directed at other outcomes such as cardiovascular events, cognitive insufficiency, disability, and mortality if these pose a greater risk to the patient than progression of kidney disease. Changing the goals of anti-hypertensive therapy may in some instances permit greater flexibility in choice of anti-hypertensive regimen.[22] The potential burden of using an ACEI or ARB must also be factored into the decision as to whether to prescribe these in preference to other agents. Prescription of ACEI and ARB in patients with CKD mandates careful monitoring for acute renal failure and hyperkalemia often requiring extra laboratory testing and clinic visits after initiation of these agents and after any change in dose. In addition, administration of these agents in patients with CKD often requires dietary modification and chronic administration of ion-exchange resins, and can also limit the use other medications that also raise serum potassium (*e.g.,* spironolactone).[15] Thus, in deciding whether to treat an older patient with CKD with an ACEI or ARB to slow progression of CKD, the clinician should consider whether the patient has proteinuria, whether their CKD is clearly progressive, whether they have other health concerns or priorities that might make another anti-hypertensive agent preferable, and whether the additional burden that these agents may impose are justified and acceptable to the patient.

CONCLUSION

Current guidelines for BP targets and choice of anti-hypertensive agents in patients with CKD are age neutral. Although these guidelines may be appropriate for many older patients with CKD, because of the complexity of medical decision making in the elderly, age differences in the clinical implications of CKD, and the high burden of other comorbidities in older patients with CKD, strict adherence to guidelines for the management of hypertension may not always represent the most patient-centric approach.

TAKE HOME POINTS

- Be aware that there is little evidence to support current guidelines for the management of BP in chronic kidney disease in the elderly because most trials did not include participants older than 70
- Realize that older patients with a low eGFR often have a variety of other comorbidities and competing treatment goals and that optimization of BP, particularly if the primary goal is slowing progression of CKD, may not always be the most important treatment priority for an individual patient

DISCLOSURES

Dr. O'Hare receives research support from the NIA and the CDC. She receives royalties from UpToDate.

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REVIEW QUESTIONS: HYPERTENSION, CHRONIC KIDNEY DISEASE, AND THE ELDERLY

1. An 83-yr-old woman with osteoporosis and cataracts but no other health problems has a stable eGFR of 55 ml/min per 1.73 m^2, an albumin to creatinine ratio of 22 mg/g, and a BP of 135/85 mmHg. She is not taking any BP medications. Which of the following BP management strategies do you think is most appropriate.
   a. Start an ACE inhibitor with a goal BP <130/80 mmHg
   b. Start a thiazide with a goal BP <130/80 mmHg
   c. Encourage her to follow a low sodium diet
   d. Do nothing
2. A 95-yr-old man with diabetes, an eGFR of 24 ml/min per 1.73 m^2, and 5 g/d of proteinuria that is presumed to be caused by diabetic nephropathy has a BP of 170/85 mmHg and a pulse of 60. His serum potassium is 4.5 mEq/L and his urine sediment is bland. He has no other comorbidities and lives independently. He is taking amlodopine 10 mg, lasix 40 mg, and metoprolol 25 mg twice daily. His primary care provider sends him to you for advice on how to manage his BP. The patient is already following a low sodium diet and walks daily. Which of the following strategies do you think is most appropriate.
   a. Start an ACE inhibitor and see him back in 1 to 2 wk for follow-up on his serum creatinine and potassium
   b. Start minoxidil or hydralazine
   c. Leave well alone because this is a normal BP for his age and adding another BP medication may cause more harm than good
   d. Start an ACE inhibitor and an ARB for control of both BP and proteinuria and see him back in 1 to 2 wk for follow-up of his serum creatinine and potassium