

What should the blood pressure be in patients with chronic kidney disease?

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The Modification of Diet in Renal Disease (MDRD) Study randomized 840 patients, with nondiabetic stage 3 to 4 chronic kidney disease to a blood pressure of less than 140/90 mmHg or to a blood pressure of 125/75 mmHg (1,2). The blood pressures achieved in this study were 133/80 mmHg versus 126/77 mmHg. The mean follow-up was 2.2 years. This study did not show a difference in death and in kidney failure between the 2 blood pressure groups. However, this study showed that in patients with proteinuria greater than 1,000 mg per day, the lower blood pressure group had a significant slower rate of decline in glomerular filtration rate (1,2).

The Ramipril Efficacy in Nephropathy (REIN-2) trial randomized 338 patients with nondiabetic stage 3 to 4 chronic kidney disease to a blood pressure of less than 140/90 mmHg or to a blood pressure of less than 130/80 mmHg (3). The blood pressures achieved in this study were 134/82 mmHg versus 130/80 mmHg. The median follow-up was 1.6 years. This study did not show a difference in death and in kidney failure between the 2 blood pressure groups (3).

The African American Study of Kidney Disease (AASK) trial randomized 1,094 patients with nondiabetic hypertensive stage 3 chronic kidney disease to a blood pressure of less than 140/90 mmHg or to a blood pressure of 125/75 mmHg (4,5). The blood pressures achieved in this study were 141/86 versus 130/78 mmHg. The median follow-up was 3.8 years. This study did not show a difference in death, end-stage renal disease, or a reduction in glomerular filtration rate of 50% or more between the 2 blood pressure groups (4). However, a subanalysis showed a reduction in this primary endpoint in patients with

proteinuria with a protein-to-creatinine ratio of more than 0.22 (5).

A meta-analysis of 2,272 patients with nondiabetic chronic kidney disease in the AASK, REIN-2, and MDRD studies found that the lower blood pressure achieved in these 3 trials of 126–130/77–80 mmHg did not improve clinical outcomes (6). However, this meta-analysis suggested that the lower blood pressure target may be beneficial in patients with chronic kidney disease with proteinuria greater than 300 to 1,000 mg daily (6).

On the basis of the available data, the International Society of Nephrology 2012 guidelines for treatment of blood pressure in patients with non-dialysis-dependent chronic kidney disease state that hypertensive patients with chronic kidney disease and albuminuria less than 30 mg per 24 hours should have their blood pressure lowered to less than 140/90 mmHg (7,8). If albuminuria greater than 30 mg per 24 hours is present, the blood pressure may be lowered to less than 130 mm/80 mmHg with a class II D indication (7,8).

A meta-analysis reported in 2013 of 11 randomized trials in 9287 patients with chronic kidney disease and 1,264 kidney failure events showed that intensive blood pressure lowering reduced the incidence of kidney failure 27% but not in patients who did not have baseline proteinuria (9). Another meta-analysis reported in 2013 included 26 randomized trials with 30,295 patients with chronic kidney disease (10). This study showed that compared with placebo, blood pressure lowering reduced the incidence of major cardiovascular events by approximately a sixth per 5 mmHg reduction in systolic blood pressure (10).

A meta-analysis reported in 2016 included 19 randomized

trials of 44,989 patients with and without chronic kidney disease in whom 2496 major cardiovascular events occurred during a mean follow-up of 3.8 years (11). Compared to a blood pressure achieved of 140/81, more intensive blood pressure lowering to an achieved blood pressure of 133/76 mmHg reduced major cardiovascular events 14%. Absolute reductions in major cardiovascular events were greatest in trials in which all enrolled patients had vascular disease, chronic kidney disease, or diabetes mellitus (11).

The most important randomized, antihypertensive clinical trial comparing a systolic blood pressure goal of less than 120 mmHg with a systolic blood pressure goal of less than 140 mmHg which included patients with chronic kidney disease is the Systolic Blood Pressure Intervention Trial (SPRINT) (12,13). This trial included 9,361 patients aged 50 years and older with a systolic blood pressure of 130 mmHg or higher and an increased cardiovascular risk but without diabetes mellitus, prior stroke, heart failure, or a left ventricular ejection fraction below 35%. The mean age was 67.9 years, 28.3% of patients were aged 75 years and older, and 28.4% of patients had chronic kidney disease with a baseline estimated glomerular filtration rate between 20 to 59 mL/min/1.73 m². Automated blood pressures were obtained in this study. The mean achieved systolic blood pressures at 1 year were 121.4 mmHg in the intensive treatment group versus 136.2 mmHg in the standard treatment group. The median follow-up was 3.26 years. The primary composite endpoint was cardiovascular death, myocardial infarction, other acute coronary syndromes, heart failure, or stroke. At follow-up, intensive treatment of blood pressure reduced the primary outcome 25% and all-cause mortality 27% in the entire group (12) and the primary outcome 34% and all-cause mortality 33% in the group aged 75 years and older (13). In the entire group of patients with chronic kidney disease, all-cause mortality was reduced 27% from 7.22% with standard blood pressure treatment to 5.26% with intensive blood pressure treatment (12). The composite renal outcome of first occurrence of a reduction in estimated glomerular filtration rate of 50% or more, long-term dialysis, or kidney transplantation was 1.1% in both blood pressure treatment groups. Intensive blood pressure treatment was also beneficial in patients with chronic kidney disease who were aged 75 years and older including those with frailty or the slowest gait speed (13).

On the basis of the data from SPRINT, the 2016 Canadian hypertension guidelines recommended lowering the systolic blood pressure to 120 mmHg or lower in

selected high-risk patients such as those with chronic kidney disease with an estimated glomerular filtration rate between 20 to 59 mL/min/1.73 m² (14,15). Automated blood pressures must be obtained in these patients. I concur with automated blood pressure measurements since they are more accurate. On the basis of the current available data, I favor lowering the blood pressure in patients with chronic kidney disease to less than 130/80 mmHg.

Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, and thiazide or thiazide-like diuretics are effective in reducing cardiovascular events in patients with hypertension associated with chronic kidney disease (16,17). However, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are more effective than other antihypertensive drugs in slowing progression of chronic kidney disease with proteinuria (18,19). The combined use of an angiotensin-converting enzyme inhibitor with an angiotensin receptor blocker should be avoided (20).

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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