Rebuttal: CON Position

People with Chronic Kidney Disease Should Have a Blood Pressure Lower than 130/80 mm Hg

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To support the notion that BP among patients with CKD be lowered to <130 mm Hg, Dr Toto [1] offers the Lewington meta-analysis. This meta-analysis was limited to people with little cardiovascular disease at baseline. Few people among the million analyzed had reported CKD. Thus, the results of this meta-analysis cannot be offered as evidence to lower BP to a systolic BP <130 mm Hg among those with CKD. CKD patients were also largely excluded from the two randomized trials, Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial and Action in Diabetes and Vascular Disease: Preterax and Diamicon-MR Controlled Evaluation (ADVANCE) Trial. Thus, one cannot extrapolate the results from these trials to those with CKD.

Many observational studies suggest an association between good outcomes and systolic BP <130 mm Hg. These observational studies simply generate a hypothesis of a cause-and-effect relationship between lower BP and better outcomes that requires testing in randomized controlled trials. As I have pointed out in my review, there are few data to support a cause-and-effect relationship between targeting a lower BP and better outcomes. The long-term follow-up of the MDRD Study and the AASK Trials were observational in nature. Likewise, the two randomized trials, Reduction in Endpoints in NIDDM with the Angiotensin Receptor Blocker Losartan (RENAAL) and Irbesartan Diabetic Nephropathy Trial (IDNT) did not test the hypothesis of BP goals in

CKD patients; post-hoc analyses of these trials were observational in nature. Therefore, these data cannot be used to offer ‘powerful evidence’ to support a lower BP goal. To explain the incongruence between observational studies and randomized trials, one must conclude that those who achieve a better BP control in observational studies also likely have better renal risk profiles and a lower cardiovascular risk that confers both renal and cardiovascular protection.

The Jafar et al. [2] meta-analysis included the results of 11 randomized trials of angiotensin-converting enzyme inhibitors to slow the progression of kidney disease. All the trials in this meta-analysis tested the notion whether angiotensin-converting enzyme inhibitor use can slow the progression of kidney disease. The majority of these trials in this meta-analysis did not randomize patients to two BP goals. Thus, the conclusions of the authors drawn from this meta-analysis on the BP goals are observational. In fact, the authors themselves conclude that ‘reverse causation cannot be excluded with certainty’. Furthermore, the adjusted relative risk (ARR) for kidney disease progression was not statistically significant when systolic BP during follow-up was between 120–129 mm Hg [ARR: 1.23 (0.63–2.40)] or 130–139 [ARR: 1.83 (0.97–3.44)]. In fact, systolic BP during follow-up <110 mm Hg was associated with kidney disease progression [ARR: 1.48 (1.07–5.77)] that was statistically significant.

Dr. Toto suggests that large-scale randomized clinical trials are needed to confirm the benefit of achieving and maintaining a systolic BP <130 mm Hg as compared to a higher systolic pressure for the purpose of reducing cardiovascular morbidity and mortality and kidney failure. I agree with his suggestion. We simply do not have sufficient evidence at this time to firmly commit a goal of systolic BP <130 mm Hg for patients with CKD.

References

- 1 Toto RD: People with chronic kidney disease should have a blood pressure lower than 130/80 mm Hg: proposition. *Am J Nephrol* 2010;32:370–373.
- 2 Jafar TH, Stark PC, Schmid CH, Landa M, Maschio G, de Jong PE, de Zeeuw D, Shahinfar S, Toto R, Levey AS, AIPRD Study Group: Progression of chronic kidney disease: The role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. *Ann Intern Med* 2003;139:244–252.