

How Low Can You Go? Blood Pressure and Mortality in Chronic Kidney Disease

Several studies document a U-shaped relationship between systolic blood pressure (SBP) and death in kidney failure (1, 2) and stage 4 and 5 chronic kidney disease (CKD) (3). Whether patients with early CKD also have increased mortality rates with both low and high SBP is unclear. In a clinical trial of proteinuric diabetic nephropathy, SBP less than 120 mm Hg or diastolic blood pressure (DBP) less than 85 mm Hg were associated with adverse cardiovascular outcomes (4). In other hypertensive populations, low DBP has been associated with increased risk for death (5). Low DBP may exert its ill effects through decreasing diastolic filling of the coronary arteries. However, low DBP may be a marker of the severity of vascular disease or vascular stiffness rather than a modifiable risk factor.

The randomized trials that have primarily influenced guideline recommendations (6) on blood pressure (BP) targets in CKD had kidney disease progression as their primary outcome because they included younger persons who were more likely to develop kidney failure than to die before it occurred. These CKD progression-focused trials did not explicitly take SBP and DBP into consideration in tandem in treatment algorithms. In addition, 2 of the trials targeted mean arterial pressure, whereas another targeted DBP (7). No randomized, controlled trials of BP targets in CKD have focused on the elderly or used cardiovascular disease or death as the primary outcome.

Current guidelines contain limited instruction about how to incorporate combinations of SBP and DBP as treatment targets. The Kidney Disease: Improving Global Outcomes Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease recommends a BP target of less than 140/90 mm Hg in persons without proteinuria and cautions that low DBP may be associated with adverse outcomes (6). It neither addresses targeting SBP and DBP together nor cites lower limits for SBP or DBP, acknowledging a lack of evidence. If one assumes that SBP and DBP move in tandem, is it preferable to have a BP of 150/70 mm Hg (not meeting SBP guideline targets) or one that is 10 mm Hg lower in each metric at 140/60 mm Hg (meeting the SBP target but with lower DBP)? Available trials cannot answer this question.

In this issue, Kovesdy and colleagues (8) add to the observational evidence on this topic by examining more than 650 000 U.S. veterans with CKD, a mean age of 73.8 years, and a mean glomerular filtration rate (GFR) of 50.4 mL/min per 1.73 m². They evaluated the associations of combinations of SBP and DBP at baseline and over time with death. The mortality rate was expectedly high in this elderly population with CKD. More than one third died during a median follow-up of 5.8 years. Data are not pro-

vided on kidney failure rates, but more than 62.3% had stage 3A CKD (eGFR, 45 to 59 mL/min per 1.73 m²); based on previous reports, mortality rates were probably several-fold higher than kidney failure rates (9), emphasizing the difference in this Veterans Affairs population versus those in randomized trials that evaluated BP targets in CKD.

When SBP and DBP were considered separately, U-shaped associations with death were seen for both SBP and DBP. Of note, BP combinations of 130 to 159/70 to 89 mm Hg were associated with the lowest risk for death. Having an SBP less than 130 mm Hg—a seemingly acceptable BP for the CKD population—was associated with greater risk for death across all DBP categories. Moreover, with observed BP combinations that included DBP less than 70 mm Hg (regardless of SBP), “better controlled hypertension” (defined by a 10-mm Hg lower SBP and DBP) was associated with increased mortality rates.

These are observational data with attendant limitations. Lower SBP and DBP may be markers of the severity of chronic illness or vascular disease. The descriptive analyses that reveal a much greater prevalence of cardiovascular disease in patients with BP less than 120/80 mm Hg, as well as the remarkable attenuation in the adjusted analyses, which raise the concern of residual confounding, support this argument. For example, a BP combination of 140 to 149/60 to 69 mm Hg is associated with a 62% greater risk over the reference combination of 140 to 149/80 to 89 mm Hg before adjustment and only a 9% greater risk after adjustment. It may not be the BP combination per se but the characteristics of the persons with that combination that lead to greater mortality rates. Also, the assumption outlined previously and implied by Kovesdy and colleagues (that DBP and SBP move in tandem with treatment) may not necessarily be the case. Translating these findings into practice is challenging.

In addition, these findings may not generalize beyond older white men with stage 3A CKD, and the fact that only a small percentage of persons had proteinuria measurements makes it difficult to draw any conclusions regarding applicability to proteinuric CKD. Are these findings unique to CKD or are they consistent in the Veterans Affairs population, regardless of GFR and proteinuria? It would also be useful to evaluate the relationship of BP combinations with kidney disease outcomes.

SPRINT (Systolic Blood Pressure Intervention Trial) (www.sprinttrial.org) will answer some questions about BP targets in CKD because approximately 3000 persons with CKD are enrolled and randomly assigned to a target SBP of less than 120 mm Hg versus a target SBP of less than 140 mm Hg. However, because SPRINT focuses on SBP

Baby pull yo'pants up



(Squeaky Voice)

How low can you go?(x8) BUT, how low can you go
Lower than yo' mamas ever seen it in her lifetime
Baby pull yo'pants up (Shawna)
Luda)

How low can you go?(x8) She can go lower than I ever really thought
she could

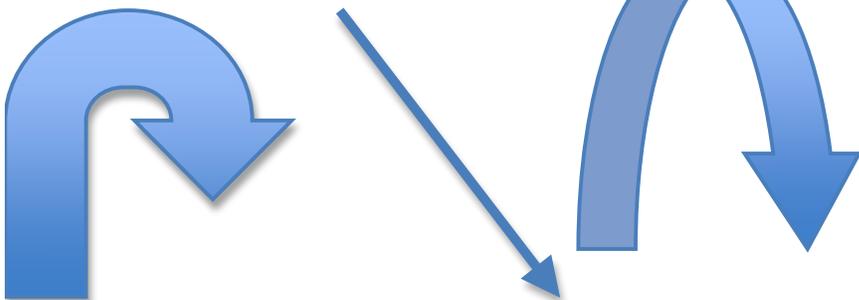
Face down, ass up

The top of yo booty jigglin' out yo'jeans I like it when I see you do it
Better than I ever seen it done before

I could go low, (go low) lower than you know,

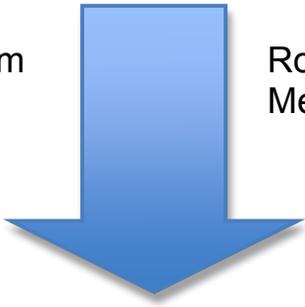
Go low,(go low) lower

than you know,



Baby pull yo'pants up

Kim



Rosenfield/Annals of Internal
Medicine/Ludacris/November Task 2013

