

Blood Pressure and Mortality among ESRD Patients: All Patients Are Not Created Equal

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The annual risk for mortality is extremely high for patients who have ESRD and are treated with dialysis in the United States,¹ and cardiovascular disease persists as their most common cause of death.² Hypertension affects the majority of hemodialysis patients, and most have what would be considered uncontrolled hypertension.³ However, appropriate BP targets for these patients remain uncertain and have largely been extrapolated from studies conducted of the general population. The Kidney Disease Outcomes Quality Initiative (KDOQI) Work Group on this subject offered an opinion of “a reasonable goal is predialysis BP <140/90 mmHg,” but the evidence to support their statement was reported as weak.⁴ The weakness of this conclusion stems partly from the exclusion of patients with ESRD from randomized trials involving antihypertensive drugs and BP targets, thereby leaving nephrologists to rely on observational data for guidance on the best approach to manage BP in dialysis patients.

Adding to the problem, these epidemiologic data are not always in agreement in their reported relationship between BP and mortality, and their findings vary on a number of factors, including when BP was analyzed (before *versus* after dialysis), whether early (1 to 2 years) *versus* late (>3 years) mortality was assessed, and whether pulse pressure was included in the analysis.^{5–9} Moreover, studies often presume that all patients with ESRD are alike despite their differences in age, gender, race, ethnicity, comorbid illnesses, socioeconomic status, and geographic location, just to name a few.

In this issue of *JASN*, Myers *et al.*¹⁰ critically examine three important patient factors—age, race, and diabetes status—to determine whether they modify the relationship between BP

and mortality among dialysis patients. Studied patients were new to hemodialysis, had survived at least 150 days from their first outpatient dialysis, had recorded predialysis BP, and were followed for a median of 1.5 years.

Several findings in this study are worthy of comment. First, the increased mortality among dialysis patients that associated with low systolic BP (SBP) in other studies^{9,11,12} was most pronounced among older patients and those with diabetes. It is probable that older patients and those with diabetes had a greater burden of severe cardiac disease (that was not measured) than their counterparts, which would place them at increased risk for death. Second, Myers *et al.* also observed that high SBP was associated with mortality only among younger hemodialysis patients, a finding that was independent of race or diabetes, suggesting that younger people with ESRD may be more similar to the general population in their risk factors for death. Third, Meyers *et al.* confirmed the long-known survival advantage for black patients who are on dialysis¹³ to be limited to older patients.

Although this is certainly one of the best observational studies to pay attention to how outcomes are different in certain patient groups, more guidance is needed. Perhaps we should be less aggressive with BP in older patients or those with diabetes and more aggressive with younger patients, but how should we treat a patient with comorbid illnesses, systolic dysfunction,¹⁴ high intradialytic weight gain, intradialytic hypotension,¹⁵ and medication nonadherence (none of which were analyzed in this study)? How do we address BP in the newly initiated hemodialysis patient knowing that approximately one in 17 will die in the first 90 days after starting dialysis,¹⁶ long before the 150 day cut point analyzed in this study? If a patient has congestive heart failure, then which approach do we take,¹⁴ and what is the role of cardiac biomarkers?¹⁷ Hypotension is a risk factor for death in patients with heart failure in the general population.¹⁸ However, there are no guidelines regarding which dialysis patients should be systematically evaluated for heart failure.⁴ Therefore, it is likely that we are underidentifying patients who are at increased risk for the deleterious effects of lower BP.

Myers *et al.*¹⁰ conclude that trials aimed at identifying optimal BP targets in ESRD should take into account age and presence of diabetes. This raises the important question of why have there not been randomized, controlled trials? The primary cause may be lack of interest in such trials. Short of the National Institutes of Health, who will fund a trial of BP targets not focused on specific medications, especially when most dialysis patients are on multiple antihypertensive agents? Design challenges may limit feasibility. Some patients, for example, may not be able to achieve the BP target to which they are randomly assigned, especially when other issues, such as ultrafiltration goals, are pressed simultaneously.

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Furthermore, such targets may impose additional costs in the form of added medications or longer dialysis treatment times. Would such a trial be ethical, for example, randomly assigning a patient to a predialysis SBP of >160 or 180 mmHg even when clinical evidence suggests that they are in a group shown to have high mortality when BP is high? Some nephrologists may find this unacceptable.

The lack of trials and the dilemma surrounding whether they could or should be conducted are cause for considering alternative methods for answering the question of BP targets in ESRD. Congress, in the American Recovery and Reinvestment Act of 2009, requested that the Institute of Medicine define national priorities for comparative effectiveness research aimed at determining *which treatment works best, for whom, and under what circumstances*, and they called for new, more robust data and methods, including efficient clinical trials, to determine effectiveness and safety of interventions.¹⁹ One of their top priorities was in the area of cardiovascular disease and ESRD. Provoked by the work of Myers *et al.* and the Institute of Medicine, let's hope that soon we will generate the evidence needed to guide the often complicated BP management of our patients.

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DISCLOSURES

None.

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See related article, “Age, Race, Diabetes, Blood Pressure, and Mortality among Hemodialysis Patients,” on pages 1970–1978.