

- Balasubramaniam S, Nurutdinova D, Xian H, Stroupe K, Abbott KC, Eisen S: Rate of kidney function decline associates with mortality. *J Am Soc Nephrol* 21: 1961–1969, 2010
11. Lely AT, van der Kleij FG, Kistemaker TJ, Apperloo AJ, de Jong PE, de Zeeuw D, Navis G: Impact of the preintervention rate of renal function decline on outcome of renoprotective intervention. *Clin J Am Soc Nephrol* 3: 54–60, 2008
  12. Matsushita K, Selvin E, Bash LD, Franceschini N, Astor BC, Coresh J: Change in estimated GFR associates with coronary heart disease and mortality. *J Am Soc Nephrol* 20: 2617–2624, 2009
  13. Rifkin DE, Shlipak MG, Katz R, Fried LF, Siscovick D, Chonchol M, Newman AB, Sarnak MJ: Rapid kidney function decline and mortality risk in older adults. *Arch Intern Med* 168: 2212–2218, 2008
  14. Shlipak MG, Katz R, Kestenbaum B, Siscovick D, Fried L, Newman A, Rifkin D, Sarnak MJ: Rapid decline of kidney function increases cardiovascular risk in the elderly. *J Am Soc Nephrol* 20: 2625–2630, 2009
  15. Xie D, Joffe MM, Brunelli SM, Beck G, Chertow GM, Fink JC, Greene T, Hsu CY, Kusek JW, Landis R, Lash J, Levey AS, O'Conner A, Ojo A, Rahman M, Townsend RR, Wang H, Feldman HI: A comparison of change in measured and estimated glomerular filtration rate in patients with nondiabetic kidney disease. *Clin J Am Soc Nephrol* 3: 1332–1338, 2008
  16. Hallan SI, Ritz E, Lydersen S, Romundstad S, Kvenild K, Orth SR: Combining GFR and albuminuria to classify CKD improves prediction of ESRD. *J Am Soc Nephrol* 20: 1069–1077, 2009

See related article, "Rate of Kidney Function Decline Associates with Mortality," on pages 1961–1969.

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

Deidra C. Crews\* and Neil R. Powe†

\*Department of Medicine, Johns Hopkins University, Baltimore, Maryland; and †Department of Medicine, University of California, San Francisco, and San Francisco General Hospital, San Francisco, California

*J Am Soc Nephrol* 21: 1816–1818, 2010.  
doi: 10.1681/ASN.2010090971

The annual risk for mortality is extremely high for patients who have ESRD and are treated with dialysis in the United States,<sup>1</sup> and cardiovascular disease persists as their most

common cause of death.<sup>2</sup> Hypertension affects the majority of hemodialysis patients, and most have what would be considered uncontrolled hypertension.<sup>3</sup> 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.<sup>4</sup> 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.<sup>5–9</sup> 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.*<sup>10</sup> 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<sup>9,11,12</sup> 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 dialysis<sup>13</sup> 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,<sup>14</sup> high intradialytic weight gain, intradialytic hypotension,<sup>15</sup> and medication nonad-

Published online ahead of print. Publication date available at www.jasn.org.

**Correspondence:** Dr. Deidra C. Crews, Division of Nephrology, Department of Medicine, Johns Hopkins University School of Medicine, 301 Mason F. Lord Drive, Suite 2500, Baltimore, MD 21224. Phone: 410-550-2820; Fax: 410-550-7950; E-mail: dcrews1@jhmi.edu

Copyright © 2010 by the American Society of Nephrology

herence (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,<sup>16</sup> long before the 150 day cut point analyzed in this study? If a patient has congestive heart failure, then which approach do we take,<sup>14</sup> and what is the role of cardiac biomarkers?<sup>17</sup> Hypotension is a risk factor for death in patients with heart failure in the general population.<sup>18</sup> However, there are no guidelines regarding which dialysis patients should be systematically evaluated for heart failure.<sup>4</sup> Therefore, it is likely that we are underidentifying patients who are at increased risk for the deleterious effects of lower BP.

Myers *et al.*<sup>10</sup> 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. 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.<sup>19</sup> 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.

## ACKNOWLEDGMENTS

D.C.C. is supported by the Harold Amos Medical Faculty Development Program of the Robert Wood Johnson Foundation. N.R.P. is supported, in part, by grant K24 DK 02643 from the National

Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health.

## DISCLOSURES

None.

## REFERENCES

- Foley RN, Hakim RM: Why is the mortality of dialysis patients in the United States much higher than the rest of the world? *J Am Soc Nephrol* 20: 1432–1435, 2009
- US Renal Data System: *USRDS 2008 Annual Data Report: Atlas of End-Stage Renal Disease in the United States*, Bethesda, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2008
- Agarwal R, Nissenson AR, Battle D, Coyne DW, Trout JR, Warnock DG: Prevalence, treatment, and control of hypertension in chronic hemodialysis patients in the United States. *Am J Med* 115: 291–297, 2003
- K/DOQI Workgroup: K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. *Am J Kidney Dis* 45[Suppl 3]: S1–S153, 2005
- Stidley CA, Hunt WC, Tentori F, Schmidt D, Rohrscheib M, Paine S, Bedrick EJ, Meyer KB, Johnson HK, Zager PG: Changing relationship of blood pressure with mortality over time among hemodialysis patients. *J Am Soc Nephrol* 17: 513–520, 2006
- Foley RN, Herzog CA, Collins AJ: Blood pressure and long-term mortality in United States hemodialysis patients: USRDS Waves 3 and 4 Study. *Kidney Int* 62: 1784–1790, 2002
- Klassen PS, Lowrie EG, Reddan DN, DeLong ER, Coladonato JA, Szczech LA, Lazarus JM, Owen WF Jr: Association between pulse pressure and mortality in patients undergoing maintenance hemodialysis. *JAMA* 287: 1548–1555, 2002
- Mazzuchi N, Carbonell E, Fernandez-Cean J: Importance of blood pressure control in hemodialysis patient survival. *Kidney Int* 58: 2147–2154, 2000
- Port FK, Hulbert-Shearon TE, Wolfe RA, Bloembergen WE, Golper TA, Agodoa LY, Young EW: Predialysis blood pressure and mortality risk in a national sample of maintenance hemodialysis patients. *Am J Kidney Dis* 33: 507–517, 1999
- Myers OB, Adams C, Rohrscheib MR, Servilla KS, Miskulin D, Bedrick EJ, Zager PG: Age, race, diabetes, blood pressure, and mortality among hemodialysis patients. *J Am Soc Nephrol* 21: 1970–1978, 2010
- Zager PG, Nikolic J, Brown RH, Campbell MA, Hunt WC, Peterson D, Van Stone J, Levey A, Meyer KB, Klag MJ, Johnson HK, Clark E, Sadler JH, Teredesai P: “U” curve association of blood pressure and mortality in hemodialysis patients. Medical Directors of Dialysis Clinic, Inc. *Kidney Int* 54: 561–569, 1998
- Chang TI, Friedman GD, Cheung AK, Greene T, Desai M, Chertow GM: Systolic blood pressure and mortality in prevalent haemodialysis patients in the HEMO study. *J Hum Hypertens* April 22, 2010 [epub ahead of print]
- Alves TP, Wang X, Wright JT Jr, Appel LJ, Greene T, Norris K, Lewis J: Rate of ESRD exceeds mortality among African Americans with hypertensive nephrosclerosis. *J Am Soc Nephrol* 21: 1361–1369, 2010
- de Mattos AM, Siedlecki A, Gaston RS, Perry GJ, Julian BA, Kew CE 2nd, Deierhoi MH, Young C, Curtis JJ, Iskandrian AE: Systolic dysfunction portends increased mortality among those waiting for renal transplant. *J Am Soc Nephrol* 19: 1191–1196, 2008
- Palmer BF, Henrich WL: Recent advances in the prevention and management of intradialytic hypotension. *J Am Soc Nephrol* 19: 8–11, 2008

16. Soucie JM, McClellan WM: Early death in dialysis patients: Risk factors and impact on incidence and mortality rates. *J Am Soc Nephrol* 7: 2169–2175, 1996
17. Wang AY, Lai KN: Use of cardiac biomarkers in end-stage renal disease. *J Am Soc Nephrol* 19: 1643–1652, 2008
18. Raphael CE, Whinnett ZI, Davies JE, Fontana M, Ferenczi EA, Manisty CH, Mayet J, Francis DP: Quantifying the paradoxical effect of higher systolic blood pressure on mortality in chronic heart failure. *Heart* 95: 56–62, 2009
19. Institute of Medicine: *Initial National Priorities for Comparative Effectiveness Research*, Washington, DC, National Academies Press, 2009

---

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