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Peridialytic, Intradialytic, and Interdialytic Blood Pressure Measurement in Hemodialysis Patients

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Hypertension is highly prevalent and frequently uncontrolled in hemodialysis (HD) patients¹, and meta-analyses of randomized controlled trials show that the treatment of HD patients with antihypertensive medications is associated with improved cardiovascular outcomes^{2,3} which remain a leading cause of death in HD patients⁴. Nonetheless, there is no consensus on whether to lower elevated blood pressure (BP) among HD patients and to what level should BP be targeted^{5,6}. This is in large part due to difficulties associated with accurate assessment of BP among HD patients^{7–10}.

Peridialytic BP measurements form the basis of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines¹¹ and are used for management of HD patients as well as epidemiologic studies because of easy availability in electronic databases of large dialysis chains; these are the BP measurements performed by dialysis unit staff shortly before and after the HD session. Thus, peridialytic BP recordings, which are often obtained without attention to methodology of measurement, have been used in the large cohort studies which have found a reverse epidemiology, where lower BP has been associated with higher mortality rates in HD patients^{6,12,13}. Routine peridialytic BP recordings are highly variable and poorly reproducible, whether these assessments are performed in carefully controlled research settings or in larger epidemiologic studies^{14,15}. Even when assessed using standard measurement methods, peridialytic BP recordings do not correlate well with end organ damage such as left ventricular hypertrophy (LVH) or cardiovascular outcomes^{16,17}. In fact, cohort studies suggest that achieving recommended peridialysis BP targets is associated with increased frequency of intradialytic hypotension¹⁸. Not surprisingly, there is poor agreement between routine peridialytic BP and the gold standard of BP measurement—interdialytic ambulatory blood pressure monitoring⁸.

The diagnostic performance of peridialytic BP recordings can be improved by consideration of intradialytic recordings¹⁹. Intradialytic BP is a recording made on HD, typically every 30 minutes via an automatic cuff attached to the HD machine. When diagnosing hypertension using ambulatory BP as a gold standard, average intradialytic BP when considered together with peridialytic BP has greater diagnostic value compared to peridialytic BP recordings alone¹⁹. However, since calculating an average is time consuming and impractical at the bedside, the median intradialytic BP (which is an adequate measure for central tendency and is close to

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the mean in normally distributed data) from a single HD session also appears appropriate for diagnosis of hypertension. It is possible that intradialytic BP correlates better with ambulatory BP over peridialytic BP because the latter, similar to interdialytic BP, samples the patient over a range of extracellular fluid volume and uremic states, albeit during the condensed time span of the HD session.

The third type of BP measurement is interdialytic, which can be obtained by ambulatory BP monitoring or by self-measurement by the patient through home BP measurements^{20–22}. Regardless of the technique of interdialytic BP assessment, these measurements appear to carry greater prognostic information compared to peridialytic recordings¹⁷. For example, interdialytic ambulatory BP is valid²³, reproducible²⁴, correlates with echocardiographic evidence of LVH,¹⁶ and is a predictor of increased mortality in HD patients¹⁷. Similarly, increased home BP has been shown to correlate with LVH and with increased cardiovascular and all-cause mortality in HD patients^{16,17}. The superiority of these methods is not just dependent on their greater number of measurements, because the interdialytic BP measures retain their correlation with all-cause mortality even if a smaller number of randomly chosen measurements are analyzed²⁵. It is felt that the interdialytic BP measurements are superior because they provide a more accurate reflection of the patient's BP burden over time, and that this burden is sampled over the range of extracellular fluid volume and uremic states, from the nadir shortly after a HD session to the zenith just prior to the next HD session^{26,27}. Ambulatory BP monitoring can be cumbersome for some patients to perform which is perhaps the main reason why the readily available peridialytic BP is still the primary measure used for diagnosing and treating hypertension in HD patients. However, home BP measurement changes also track well with changes in ambulatory BP recordings, therefore home BP can be used to make therapeutic decisions²⁸.

In this issue of the *American Journal of Kidney Diseases*, Inrig and colleagues report that a rising peridialytic systolic BP in incident HD patients with normal pre-HD systolic BP is significantly associated with increased mortality at two years²⁹. This observation comes on the heels of a post hoc analysis of a randomized trial where the same author reported increased 6 month mortality rates with rising peridialytic systolic BP³⁰. Given that both are observational studies, which do not prove cause and effect, the interpretation of these findings requires two approaches. The questions we pose are first, if the findings are causally related why should they be so, and second, if the findings are unrelated what could underlie the observations.

We, like the authors, cannot think of a plausible direct causal link between rising BP and increased mortality. It thus follows that the observed increase in mortality would not be mitigated if the rise in peridialytic BP were prevented through measures such as the predialysis use of antihypertensive medications.

If the findings are causally unrelated, there are several possible reasons for this association (Box 1). *First*, as the authors speculate, rising BP may be a manifestation of endothelin excess that is associated with endothelial dysfunction and atherosclerosis which may manifest in the observed increased mortality³¹. *Second*, the observed increase in mortality was limited to patients with low normal pre-HD BP who also had rising peridialytic BP. These patients often are clinically dwindling due to advanced chronic disease. In fact, the patients with rising peridialytic systolic BP_[DBP] are noted by Inrig et al to have significantly lower interdialytic weight gain and serum phosphorus, consistent with decreased oral intake. Similarly, these patients have significantly lower body mass index and serum creatinine, consistent with more wasting than those patients without a rise in peridialytic BP. Lastly they are noted to have significantly lower serum albumin, consistent with more inflammation. Perhaps the increased mortality in this population is due to advanced chronic illness that isn't accounted for in the statistical adjustments³². *Third*, patients with normal pre-HD systolic BP may also be more

prone to intradialytic hypotension than the rest of the HD population, which might in turn be prevented or treated with hypernatremic dialysate, frequent cessation of ultrafiltration, and saline infusions. These interventions can result in an increased post-HD systolic BP and leave the patient volume overloaded, which itself is another potential etiology of the observed increased mortality. Unfortunately, intradialytic BP recordings weren't available for investigation of intradialytic hypotensive episodes. *Fourth*, if these patients start HD with a normal systolic BP and finish with a higher systolic BP, their systolic BP must necessarily decrease in the interdialytic period back down to a normal value prior to their next HD session. This decreasing BP in the interdialytic period is a potential marker of volume excess³³. Given the study design we don't have measurements of the volume state or the level of their left ventricular function, either of which can predict mortality³⁴. *Fifth*, we do not know how reproducible the observed rises in peridialytic BP recordings are, as they are from only three consecutive HD sessions and peridialytic BP recordings themselves are prone to high variability²⁴.

Notwithstanding these limitations, the paper by Inrig et al is important because it calls attention to BP assessment in HD patients, and it looks beyond conventional peridialytic BP to analyzing patterns of peridialytic BP. Whereas interdialytic ambulatory BP measurement is the gold standard for the diagnosis of hypertension in HD patients, its implementation can be difficult and it isn't readily available in most HD units. The routine use of peridialytic BP measurement represents the other end of the spectrum, as these BP recordings are easily obtained but have lesser reproducibility and utility. The median of intradialytic BP measurements and peridialytic BP recordings may represent an acceptable compromise between utility and practicality.

With respect to intradialytic BP measurements, additional studies are required on multiple fronts. First, larger studies are needed to confirm the diagnostic performance of intradialytic BP recordings. Second, it is unknown whether intradialytic BP correlates with end organ damage or hard outcomes such as cardiovascular events and mortality. Third, just as this study focuses on the pattern of peridialytic BP, and as patterns of interdialytic ambulatory BP appear to be associated with volume status and arterial stiffness³⁵, the pattern of intradialytic BP warrants further investigation.

There is still no consensus on the best overall measure of BP in HD patients from the point of view of patients, practitioners, or the healthcare system, but based on current evidence we must look beyond routine peridialytic BP. Intradialytic BP is one candidate for a compromise between scientific rigor and everyday ease-of-use. However, a paradigm shift appears to be indicated³⁶; BP obtained during dialysis should be used to ensure hemodynamic stability and home BP monitoring for diagnosing and treating hypertension among hemodialysis patients^{3,37}.

Box 1

Possible explanations for the association between rising peridialytic blood pressure and mortality in patients with low-normal pre-hemodialysis systolic blood pressure

1. Rising BP is a marker of endothelial dysfunction.
2. Low pre-HD BP is a marker of advanced chronic illness.
3. Low pre-HD BP is a marker of susceptibility to intradialytic hypotension, which when treated leads to volume overload.
4. Rising peridialytic BP is itself a marker of volume overload.

5. Rising peridialytic BP is not reproducible within a given patient, and therefore the observed association with mortality is a random event.

Abbreviations: HD, hemodialysis; BP, blood pressure.

References

1. Agarwal R, Nissenson AR, Battle D, et al. Prevalence, treatment, and control of hypertension in chronic hemodialysis patients in the United States. *Am J Med* 2003;115:291–297. [PubMed: 12967694]
2. Heerspink HJ, Ninomiya T, Zoungas S, et al. Effect of lowering blood pressure on cardiovascular events and mortality in patients on dialysis: a systematic review and meta-analysis of randomised controlled trials. *Lancet* 2009;373:1009–1015. [PubMed: 19249092]
3. Agarwal R, Sinha AD. Cardiovascular protection with antihypertensive drugs in dialysis patients: systematic review and meta-analysis. *Hypertension* 2009;53:860–866. [PubMed: 19273737]
4. Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation* 2003;108:2154–2169. [PubMed: 14581387]
5. Foley RN, Agarwal R. Hypertension is harmful to dialysis patients and should be controlled. *Semin Dial* 2007;20:518–522. [PubMed: 17991197]
6. Agarwal R. Hypertension and survival in chronic hemodialysis patients-Past lessons and future opportunities. *Kidney Int* 2005;67:1–13. [PubMed: 15610223]
7. Agarwal R. Systolic hypertension in hemodialysis patients. *Semin Dial* 2003;16:208–213. [PubMed: 12753679]
8. Agarwal R, Peixoto AJ, Santos SF, et al. Pre and post dialysis blood pressures are imprecise estimates of interdialytic ambulatory blood pressure. *Clin J Am Soc Nephrol* 2006;1:389–398. [PubMed: 17699236]
9. Li Z, Lacson E Jr, Lowrie EG, et al. The epidemiology of systolic blood pressure and death risk in hemodialysis patients. *Am J Kidney Dis* 2006;48:606–615. [PubMed: 16997057]
10. Lacson E Jr, Lazarus JM. The association between blood pressure and mortality in ESRD-not different from the general population? *Semin Dial* 2007;20:510–517. [PubMed: 17991196]
11. K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. *Am J Kidney Dis* 2005;45:S1–153.
12. Port FK, Hulbert-Shearon TE, Wolfe RA, et al. Predialysis blood pressure and mortality risk in a national sample of maintenance hemodialysis patients. *Am J Kidney Dis* 1999;33:507–517. [PubMed: 10070915]
13. Zager PG, Nikolic J, Brown RH, et al. “U” curve association of blood pressure and mortality in hemodialysis patients. Medical Directors of Dialysis Clinic, Inc [published erratum appears in *Kidney Int* 1998 Oct;54(4):1417]. *Kidney Int* 1998;54:561–569. [PubMed: 9690224]
14. Agarwal R, Andersen MJ, Bishu K, et al. Home blood pressure monitoring improves the diagnosis of hypertension in hemodialysis patients. *Kidney Int* 2006;69:900–906. [PubMed: 16518349]
15. Rohrscheib MR, Myers OB, Servilla KS, et al. Age-related blood pressure patterns and blood pressure variability among hemodialysis patients. *Clin J Am Soc Nephrol* 2008;3:1407–1414. [PubMed: 18701616]
16. Agarwal R, Brim NJ, Mahenthiran J, et al. Out-of-hemodialysis-unit blood pressure is a superior determinant of left ventricular hypertrophy. *Hypertension* 2006;47:62–68. [PubMed: 16344376]
17. Alborzi P, Patel N, Agarwal R. Home blood pressures are of greater prognostic value than hemodialysis unit recordings. *Clin J Am Soc Nephrol* 2007;2:1228–1234. [PubMed: 17942773]
18. Davenport A, Cox C, Thuraishingham R. Achieving blood pressure targets during dialysis improves control but increases intradialytic hypotension. *Kidney Int* 2007;73:759–764. [PubMed: 18160959]
19. Agarwal R, Metiku T, Tegegne GG, et al. Diagnosing hypertension by intradialytic blood pressure recordings. *Clin J Am Soc Nephrol* 2008;3:1364–1372. [PubMed: 18495949]

20. Peixoto AJ, White WB. Circadian blood pressure: clinical implications based on the pathophysiology of its variability. *Kidney Int* 2007;71:855–860. [PubMed: 17377513]
21. Thompson AM, Pickering TG. The role of ambulatory blood pressure monitoring in chronic and end-stage renal disease. *Kidney Int* 2006;70:1000–1007. [PubMed: 16850026]
22. Agarwal R. Role of home blood pressure monitoring in hemodialysis patients. *Am J Kidney Dis* 1999;33:682–687. [PubMed: 10196009]
23. Peixoto AJ, Gray TA, Crowley ST. Validation of the SpaceLabs 90207 ambulatory blood pressure device for hemodialysis patients. *Blood Press Monit* 1999;4:217–221. [PubMed: 10547641]
24. Peixoto AJ, Santos SF, Mendes RB, et al. Reproducibility of ambulatory blood pressure monitoring in hemodialysis patients. *Am J Kidney Dis* 2000;36:983–990. [PubMed: 11054355]
25. Agarwal R, Andersen MJ, Light RP. Location Not Quantity of Blood Pressure Measurements Predicts Mortality in Hemodialysis Patients. *Am J Nephrol* 2007;28:210–217. [PubMed: 17960059]
26. Kelley K, Light RP, Agarwal R. Trended cosinor change model for analyzing hemodynamic rhythm patterns in hemodialysis patients. *Hypertension* 2007;50:143–150. [PubMed: 17515445]
27. Agarwal R, Light RP. Chronobiology of Arterial Hypertension in Hemodialysis Patients: Implications for Home Blood Pressure Monitoring. *Am J Kidney Dis*. 2009
28. Agarwal R, Satyan S, Alborzi P, et al. Home blood pressure measurements for managing hypertension in hemodialysis patients. *Am J Nephrol* 2009;30:126–134. [PubMed: 19246891]
29. Inrig JK, Patel UD, Toto RD, Szczech LA. Association of Blood Pressure Increases during Hemodialysis with 2-year Mortality in Incident Hemodialysis Patients: A Secondary Analysis of the Dialysis Morbidity and Mortality Wave 2 Study. *AJKD*. 2009
30. Inrig JK, Patel UD, Gillespie BS, et al. Relationship between interdialytic weight gain and blood pressure among prevalent hemodialysis patients. *Am J Kidney Dis* 2007;50:108–118. [PubMed: 17591530]
31. Chou KJ, Lee PT, Chen CL, et al. Physiological changes during hemodialysis in patients with intradialysis hypertension. *Kidney Int* 2006;69:1833–1838. [PubMed: 16691262]
32. Agarwal R. Exploring the paradoxical relationship of hypertension with mortality in chronic hemodialysis. *Hemodialysis Int* 2004;8:207–213.
33. Agarwal R. Volume-Associated Ambulatory Blood Pressure Patterns in Hemodialysis Patients. *Hypertension*. 2009
34. Satyan S, Light RP, Agarwal R. Relationships of N-terminal pro-B-natriuretic peptide and cardiac troponin T to left ventricular mass and function and mortality in asymptomatic hemodialysis patients. *Am J Kidney Dis* 2007;50:1009–1019. [PubMed: 18037101]
35. Agarwal R, Light RP. Arterial stiffness and interdialytic weight gain influence ambulatory blood pressure patterns in hemodialysis patients. *Am J Physiol Renal Physiol* 2007;294:F303–F308. [PubMed: 18160623]
36. Pickering TG, Miller NH, Ogedegbe G, et al. Call to action on use and reimbursement for home blood pressure monitoring: a joint scientific statement from the American Heart Association, American Society Of Hypertension, and Preventive Cardiovascular Nurses Association. *Hypertension* 2008;52:10–29. [PubMed: 18497370]
37. Agarwal R. How should hypertension be assessed and managed in hemodialysis patients? Home BP, not dialysis unit BP, should be used for managing hypertension. *Semin Dial* 2007;20:402–405. [PubMed: 17897244]