Patient-Centered Approach for Hypertension Management in End-Stage Kidney Disease: Art or Science?

Elvira O. Gosmanova, MD, FASN,[,†] and Csaba P. Kovesdy, MD, FASN[‡,§]*

Summary: Hypertension is present in most patients with end-stage kidney disease initiating dialysis and management of hypertension is a routine but challenging task in everyday dialysis care. End-stage kidney disease patients are uniquely heterogeneous individuals with significant variations in demographic characteristics, functional capacity, and presence of concomitant comorbid conditions and their severity. Therefore, these patients require personalized approaches in addressing not only hypertension but related illnesses, while also accounting for overall prognosis and projected longevity. There are only limited clinical trial data to guide individualized blood pressure management and current guidelines are based predominantly on observational evidence and expert opinions. In this review, we reflect on the shortcomings of peridialytic blood pressure recordings and discuss an important paradigm shift toward using out-of-dialysis blood pressure for evaluating hypertension control and for making treatment decisions. In addition, we provide our personal view on blood pressure goals and summarize nonpharmacologic and pharmacologic treatment options for individualized management of hypertension in end-stage kidney disease.
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Evaluation and treatment of hypertension is a routine part of dialysis management. Hypertension is the second most common cause of end-stage kidney disease (ESKD) in the developed world and also the most common associated comorbidity in ESKD of other etiologies,[1] which is present in 90% to 95% of incident dialysis patients.[1,2] Although the prevalence of hypertension decreases 30 to 36 months after dialysis onset, hypertension continues to be observed in approximately 85% of long-term dialysis patients.[1,3] Precision medicine is becoming the focus of intense investigation in many disease states and is supported by government initiatives. Although still in early stages, personalized approaches for treating hypertension also are being investigated in the general population.[4] By using several -omics methods, promising candidate genes and gene products determining response to different antihypertensive drug classes now have been identified.[5-8] However, the validity of these genomic and nongenomic markers requires further confirmation, and their utility as a precision medicine tool will need to be evaluated in randomized controlled trials (RCTs). Unfortunately, formal precision medicine interventions have yet to be tested in patients with ESKD and cannot be used to guide therapy selection for blood pressure (BP) control in this population. Several biochemical markers, such as circulating B-type natriuretic peptides, catecholamines, and aldosterone, are being investigated in ESKD patients,[9-11] but preliminary results have focused mainly on predicting outcomes, and there are no clinical trial data on using biomarkers as a guide for antihypertensive therapy.

ESKD individuals comprise a heterogeneous group of patients regarding age and functional capacity, comorbidities and their severity, presence of residual renal function (RRF), adherence to diet and medications, and suitability for kidney transplantation. This diversity hinders the performance of sufficiently powered clinical trials that could provide guidance for hypertension treatment, yet it also demands an individualized approach for every ESKD patient. In addition, ESKD is associated with a loss of a steady state in maintaining solute and fluid balance, a cornerstone of BP regulation, because of the intermittent nature of delivered dialysis resulting in significant and cyclic BP fluctuations. This variability leads to an apparently differential and even paradoxical impact of BP obtained under different circumstances (ie, BPs obtained in or out of the dialysis unit) on patient-centered outcomes. Given the numerous limitations in the reliability of peridialytic BP recordings (see later), there is growing evidence supporting the primary role of out-of-dialysis BP for treatment decisions in ESKD.[12,13] In addition to reporting peridialytic and interdialytic methods of BP evaluation in ESKD patients and their prognostic implications, we summarize current treatment options and our proposed pathophysiology-based algorithm for a patient-centered approach for hypertension management in dialysis patients.

*Nephrology Section, Stratton VA Medical Center, Albany, NY.
†Division of Nephrology, Department of Medicine, Albany Medical College, Albany, NY.
‡Division of Nephrology, Department of Medicine, University of Tennessee Health Science Center, Memphis, TN.
§Nephrology Section, Memphis VA Medical Center, Memphis, TN.
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Address reprint requests to Csaba P. Kovesdy, MD, FASN, Division of Nephrology, University of Tennessee Health Science Center, 956 Court Ave, Memphis, TN 38153. E-mail: ckovesdy@uthsc.edu
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EVALUATION OF HYPERTENSION AND ITS CONTROL IN HEMODIALYSIS PATIENTS

Renal replacement therapy in the form of hemodialysis (HD), which is the most commonly used modality of renal replacement therapy in the United States,[1] prolongs survival and improves quality of life in ESKD patients. However, its intermittent nature makes it incapable of sustaining a true steady state that is fundamental for normal sodium and fluid balance and maintenance of BP in an adequate range. It therefore is not surprising that BP fluctuations are common in HD patients. BP tends to increase during the interdialytic period and decrease during dialysis with ultrafiltration[14,15]; nevertheless, this is not a uniform phenomenon and various patterns of BP change occurring during dialysis have been described.[16,17] However, typically it appears that the degree of BP change parallels interdialytic weight gain (IDWG) and the amount of ultrafiltration occurring during dialysis. A higher IDWG is associated with higher interdialytic and predialysis systolic BP (SBP), as well as a larger SBP reduction during dialysis.[18,19] Because IDWG can vary between different dialysis treatments in the same patient, there is also a significant intra-individual BP variation observed between dialysis visits, with one study reporting SDs in intra-individual predialysis and postdialysis SBP of 17.2 and 15.5 mm Hg, respectively.[20] Therefore, BP in hemodialysis patients constantly and cyclically fluctuates but the magnitude of these changes can be variable between dialysis treatments, making isolated BP recordings, especially those recorded in the dialysis unit, unreliable for the evaluation of the total hypertension burden.

In-Center Dialysis Blood Pressure

There are several settings where BP can be measured in HD patients: peridialytic or in-center dialysis BP; including BP before (predialysis), during, and after dialysis (postdialysis); and interdialytic or out-of-dialysis BP, including 44-hour ambulatory BP monitoring (ABPM), home BP monitoring (HBPM), and out-of-dialysis office BP. With dialysis three times per week, an average patient spends approximately 12 hours in the dialysis unit, which comprises approximately 8% of total weekly time. However, in-center dialysis BP is currently the most commonly used parameter for routine decision making about hypertension diagnosis and its control because of its convenience. It is critical to recognize that peridialytic BP is largely unstandardized (no rest period in a quiet environment, no arm support, poorly calibrated devices). In addition, technical difficulties resulting from previous and current permanent hemodialysis access in the upper arm, white-coat effect, anxiety caused by the HD procedure (access cannulation, desire to leave dialysis unit, fear of prolonged postdialytic recovery time), inadequate adherence to antihypertensive drugs or advice to hold them before dialysis, and intradialytic antihypertensive drug removal further influence peridialytic BP.[13] Hence, it is not surprising that there is a poor correlation between in-center dialysis and out-of-dialysis BP recordings. Predialysis SBP and diastolic BP (DBP) tend to overestimate ambulatory SBP and DBP, with wide agreement limits of +41.7 to −25.2 mm Hg and +23.7 to −18.9 mm Hg, respectively.[21] In contrast, postdialysis SBP and DBP underestimate ambulatory SBP and DBP, also with wide agreement limits of +33.1 to −36.3 mm Hg and +19.3 to -23.9 mm Hg, respectively.[21] Nonetheless, intradialytic hypertension defined as an SBP increase between postdialsyis and predialysis BP of more than 10 mm Hg, which is observed in approximately 10% of dialysis patients, might be a better marker of interdialytic hypertension.[17,22] In a study involving 50 HD individuals, patients with intradialytic hypertension had an average ambulatory SBP that was 13.0 mm Hg higher despite a lower predialysis SBP, as compared with patients without intradialytic hypertension.[17] Considering the complicated relationship of predialysis and postdialysis BP with ambulatory BP coupled with intra-individual peridialytic BP variability, the estimation of interdialytic BP from peridialytic BP is very imprecise. For example, in a study by Bansal et al,[23] the majority (60%) of dialysis patients with a predialysis SBP of 140 mm Hg or higher had an out-of-dialysis office SBP of less than 140 mm Hg, but another study showed that the average of all peridialytic SBP measurements over six consecutive HD treatments had the highest correlation with ABPM.[20] A cut-off SBP of greater than 140 mm Hg obtained from the average of all peridialytic SBP measurements from a single dialysis provided 80% sensitivity and 80% specificity for predicting SBP by ABPM of 135 mm Hg or greater.[20] Therefore, peridialytic BP can be a proxy of interdialytic BP only to a limited extent and out-of-dialysis BP should be favored to diagnose hypertension and to evaluate its control in dialysis patients, especially given the fact that patients spend most of their time in the out-of-dialysis setting.

Out-of-Dialysis Blood Pressure

A 24- to 44-hour ABPM performed after the first or after the midweek hemodialysis session is advocated by the recent European Renal and Cardiovascular Medicine working group as the gold standard for interdialytic BP evaluation.[13] Of note, shorter intervals of ambulatory BP recording (24, 12, and even 6 hours) retains prognostic significance for predicting all-cause mortality, as compared with 44-hour ABPM despite slight variations in mean SBP.[24] In addition, ABPM can provide important information about masked hypertension and a nocturnal dipping pattern. However, ABPM availability is limited and the method does require a patient's acceptance and adherence with the technique. Unless the nephrology community and guidelines come together and strongly advocate for