Clinical Value of Ambulatory Blood Pressure Monitoring in CKD

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Accurate measurement and classification of blood pressure (BP) are essential in managing hypertensive patients with chronic kidney disease (CKD). Guidelines and scientific statements recommend ambulatory BP monitoring (ABPM) or, when not available, home BP measurements (HBPM) to confirm the presence of hypertension and identify patients with white-coat or masked hypertension.[1,2] Because BP follows a circadian pattern, ABPM can also be used to assess diurnal BP profile, with key parameters being nighttime (sleep) BP and nocturnal BP dipping pattern (sleep-awake BP cycle). The prognostic superiority of out-of-office BP measurements over standard office-based readings has been amply demonstrated in many observational studies.[2] In patients with hypertension and CKD who are not receiving dialysis, ambulatory BP—whether it be mean 24-hour, daytime, or nighttime—is associated with hypertension-mediated target organ damage, cardiovascular (CV) events, progressive kidney disease (often leading to kidney failure), and mortality, and the adverse prognosis is robust even after adjustments for traditional risk factors including office BP.[3] CKD patients with white-coat hypertension are not at substantially higher risk for a CV event than normotensive patients,[3,4] while masked hypertension, a common finding in CKD cohorts, confers the same level of risk for adverse outcomes as sustained hypertension.[4] Reduced nocturnal BP dipping (also referred to as nondipping) is highly prevalent in hypertensive patients with CKD, accounting for more than 60% of participants in most studies and almost 90% of those with advanced CKD.[4–6] Loss of the normal diurnal variation in BP is associated with markers of kidney dysfunction, such as reduced glomerular filtration rate (GFR), albuminuria, and impaired sodium excretion, and predicts progressive deterioration in GFR (often defined as a 50% decrease) and kidney failure, even after adjusting for office BP.[3,4] These relationships have been shown to be log-linear and continuous, with no threshold level where risk increases suddenly.[2]

To facilitate the clinical application of ABPM, threshold levels of ambulatory BP that are the risk equivalent to office BP levels were derived from prospective observational studies with CV end points[2] and nondipping BP pattern was arbitrarily defined as a decrease in nocturnal BP relative to daytime BP of <10%.[1] In the article by Borrelli et al[7] published in the current issue of *AJKD*, the investigators explored the use of 2 closely related ABPM parameters, ambulatory BP (daytime and nighttime BP) and dipping status, expressed as categorical variables, to evaluate the prognosis of treated patients with hypertension and CKD who were not receiving kidney replacement therapy (dialysis or transplant). Few studies with CV and kidney outcomes have used both BP parameters in the same sample to determine their relative importance in predicting outcomes. Identifying the best BP index of risk and in what circumstances provides an opportunity to develop and test a more focused approach to treatment.

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Borrelli et al categorized the 906 hypertensive patients with CKD (stages 2-5) in their study into 1 of 4 mutually exclusive groups: ambulatory BP above or at goal (defined as daytime and nighttime systolic BP <135 mm Hg and <120 mm Hg, respectively) and nondipping or dipping (defined as night-to-day ratio of systolic BP <0.9 based on a single 24-hour ABPM performed at baseline). Study participants were followed for a median of 7.8 years. Outcomes were a kidney progression outcome (defined as a composite of ≥50% decline in estimated GFR or initiation of maintenance dialysis) and all CV events. In total there were 315 kidney progression events and 220 CV events. In line with past studies[4–6] the prevalence of nondipping was 70% and nondippers above ambulatory BP target were older, were predominantly men, had a history of diabetes or prior CV disease, and had lower estimated GFR, more proteinuria, and higher nighttime BP than dippers not at ambulatory BP goal. Not surprisingly, these patients were at highest risk for kidney disease progression and CV events. The novel findings of the study were the increased kidney as well as CV risk of nondippers at ambulatory BP goal compared to normotensive dippers, and that the increased level of risk was virtually identical to that of dippers with uncontrolled hypertension. The authors concluded that nocturnal nondipping BP pattern is an independent risk factor for adverse events among hypertensive patients with CKD and should be considered a target for therapeutic intervention to restore normal dipping status.

Despite the encouraging results, ascertaining dipping status as a treatment target is still controversial for several reasons. First, dipping status derived from a single 24-hour ABPM recording, as in the current study, is poorly reproducible.[8] This has led guideline committees and others to recommend repeat testing or extending monitoring to 48 hours to confirm the presence of nondipping.[1,2] Second, observation studies can only identify links; as such, they do not imply a reduction in adverse effects of nondipping with successful treatment.[2,3] Moreover, successful treatment of nondipping, for example by bedtime administration of antihypertensive medications, is invariably accompanied by a decrease in nocturnal BP,

making it difficult to tease out the relative contributions of these highly correlated variables to any observed benefits.[9,10] Third, in a meta-analysis of prospective studies involving patients with hypertension, dipping status remained significantly associated with total mortality or composite CV end points even with adjustment for 24-hour BP, but its inclusion did not greatly improve the model fit beyond the 24-hour BP readings.[11] In keeping with this finding, a recent randomized controlled trial of patients with advanced CKD and poorly controlled hypertension showed that the addition of chlorthalidone, a long-acting thiazide diuretic, to existing drug therapy significantly reduced ambulatory daytime and nighttime BP in parallel but did not substantially lower the high percentage of participants with nondipping BP pattern.[6] Finally, nondipping expressed as a categorical variable is not a robust measure in assessing benefits. This was apparent in chronobiology studies in which bedtime dosing of antihypertensive medications greatly improved the dipping ratio (a continuous variable) and clinical outcomes but only re-established a normal nocturnal BP dipping pattern in about one-third of patients.[9,10]

There is a growing support for out-of-office BP measurements, not only for diagnosis, but, importantly, for monitoring antihypertensive treatment after its initiation. Measurement options include ABPM, HBPM, and, more recently, small wearable devices, although the latter is still hampered by issues around accuracy, reproducibility, and calibration.[12] Guidelines recommend both ABPM and HBPM and view them as complementary procedures.[1] HBPM allows patients to monitor their BP regularly over an extended period of time and is a powerful monitoring tool when coupled with a BP telemonitoring system that provides feedback support in real time from a multidisciplinary clinical team.[1,13] It is particularly valuable in situations where there are frequent changes in antihypertensive drug treatment to improve BP control or in response to medication side effects. ABPM is less well suited for repeated monitoring because of inconvenience, cost (not a recoverable expense in many jurisdictions), and poorer patient acceptance.[2,14] Indeed, position papers and scientific statements envisage a more limited role of ABPM in the long-term management of hypertension. Situations where ABPM seems to have advantages over HBPM include assessment for nocturnal hypertension in patients at risk such as those with more advanced CKD, diabetes, or obstructive sleep apnea; evaluation of patients with symptomatic hypotension, especially when associated with severe supine hypertension; and ascertaining therapeutic coverage over 24 hours.[14,15] A major limitation of both ABPM and HBPM as the primary measurement tool in managing hypertension is the lack of clinical trials with hard outcomes using BP from these procedures to determine eligibility for treatment and goals of therapy. Current drug treatment parameters are founded on the results of multiple clinical trials that exclusively used office-based BP measurements. As such, they are widely accepted and will likely continue to inform clinical decision making until new evidence indicates otherwise.[2,14,15]

Article Information

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