Hypertension confers higher cardiovascular (CV) risks in hemodialysis (HD) patients. There are no data to guide the level to which BP should be reduced or when and where to measure BP in such patients. Unlike BP guidelines to reduce CV risk in the general population, no uniform guidelines address the HD patient. This article focuses on when and how to measure BP and efforts to quantify this measure in the HD-dependent patient. A U-shaped curve exists between BP level and mortality in HD patients, with higher mortality noted at lower levels of BP <120 mmHg and levels >180 mmHg measured before HD. Previous studies examined risk reduction through evaluating BP readings from dialysis units. Peridialysis values were biased and, thus, less representative of risk. Newer studies using home BP and ambulatory BP during 24 h have provided a narrower range of BP values that may reduce CV risk but must be tested in a clinical trial. Ambulatory BP monitoring is a growing tool for hypertension evaluation along with changes in vascular compliance; however, these methods are mainly used in research settings. Home BP values on interdialytic days are practical and also demonstrate good correlations with ambulatory readings. Aggressive volume control seems key to maintaining good BP control. Once a valid time and measure for BP is agreed on, a clinical outcome trial is needed to test its utility.

Hypertension Goals in Advanced-Stage Kidney Disease

Keith Hopkins and George L. Bakris

Department of Medicine, Section of Endocrinology, Diabetes and Metabolism, Hypertensive Diseases Unit, University of Chicago Pritzker School of Medicine, Chicago, Illinois

M more than 72 million Americans carry a diagnosis of hypertension, and an estimated 13% of these patients have stage 3 or higher chronic kidney disease (CKD) (1,2). Hypertension is the second most common cause of ESRD and together with diabetes accounts for more than two thirds of the patients who are on dialysis today (3,4).

The Seventh Joint National Committee (JNC 7) guidelines for BP classification and measurements apply to the general population, not to patients with ESRD (5). This is also true for the National Kidney Foundation guidelines (6). These guidelines recommend reduction of systolic BP (SBP) to levels <130 mmHg; the prospective data do not support this for patients who have CKD without proteinuria (7). Conversely, it is clear that reducing SBP to levels <140 mmHg is associated with a clear reduction in the incidence of stroke and CKD progression (7,8).

Although the most recent data clearly show improvement in BP control among those who are treated for hypertension, the control rates among those with advanced CKD is much lower than in the general population (2,8). Moreover, those who are in lower socioeconomic groups and do not have health care coverage have a disproportionately higher burden of poor BP control and higher rates of CKD that requires dialysis (9,10). Thus, it is imperative that reduction of SBP to levels <140 mmHg become a focal point of health care on a national, local, and personal level. Moreover, screening programs of groups that are at higher risk for CKD progression must be continued and expanded to curtail this epidemic of ESRD (11).

Unlike the general population, for which there is a clear consensus of how to measure BP and the BP goal that is needed to reduce risk, this is not the case for people who receive renal replacement therapy. Moreover, in the patient with ESRD, a consensus for how to measure BP and to which level it should be reduced has not been reached. This article discusses the evidence of when to measure BP in patients with ESRD and what the goal should be to reduce cardiovascular (CV) risk.

The recommendation for measuring BP in the general population includes the patient’s sitting quietly upright in a chair for approximately 5 min with the arm supported at heart level. In addition, an appropriately fitting sphygmomanometer cuff is recognized as vital to accurate readings (5). Conversely, there remains disagreement concerning the utility and reproducibility of such a method in hemodialysis (HD) patients. In addition, there is a question in this group as to the optimal time for BP measurement that is representative of the overall daily BP: The pre-HD, post-HD, or interdialytic reading (12). The added complexity in this subset of patients relates largely to variations in a patient’s volume between dialysis days, variability in BP measurements, and time of day when measurement is obtained. BPs measured in dialysis units are generally elevated when compared with averaged home ambulatory BP measurements (ABPMs) (13).

ABPMs are considered the gold standard for assessing overall BP in the context of CV risk (12), but does this measure apply to the ESRD population? Zoccali et al. (14) demonstrated a correlation between elevated ambulatory pressures and increased left ventricular mass (LVM) in a cohort of patients who had ESRD without diabetes, and this finding was confirmed in a more diverse population of patients with ESRD (15). That study also stressed the importance of abnormal vascular compliance as a possible marker for increased CV risk in patients...
with ESRD. Although it is widely recognized that averaging a greater number of ABPMs would give a better mean, the clinical value of ABPMs is retained even when a small number of randomly selected BPs from interdialytic ABPMs are selected to predict LVM or mortal outcomes (16).

ABPMs are known to be more representative of chronic vascular tone than are in-center values. One could easily postulate that the greater the arterial stiffness, the less likely that person is to handle large daily volume changes and the greater likelihood of a CV death. Evidence to support this hypothesis exists (17): Patients’ BPs were controlled in large part by adjustment of their dry weight; however, those whose pulse wave velocity did not decrease despite decreased BP had much higher mortality.

A meta-analysis of BP assessed at different times over days of HD indicated that pre-HD SBP overestimates ABPM values (12). These pre-HD SBPs are influenced by increased body fluid volumes, the withholding of antihypertensive medications before treatments, and a lack of standardized measurements. Post-HD measurements, although closer to the 24-h ABPM readings, underestimate ambulatory values (12). By acquiring multiple BP readings throughout the day, with special attention paid to early morning BP, when CV risks are highest, ABPMs provide data that are more representative than any singular point in ESRD.

Solid evidence to support an ideal BP range to lower CV risk in patients with ESRD does not exist. Zager et al. (18) examined mortality rates during a 5-yr period in >5400 dialysis-dependent patients. They noted that SBPs >180 mmHg (relative risk 1.73; P < 0.001) and <110 mmHg (relative risk 2.04; P = 0.001) in the post-HD period were associated with increased CV mortality. Stidley et al. (19) reevaluated the relationship between BP and mortality in two sets of Cox proportional hazards models. The >16,000 patients analyzed were similar in characteristics to the US Renal Data System’s population, although the group was overrepresented by black patients who were on HD. They noted that pre-HD BP values between 140 and 160 mmHg were not associated with increased CV mortality among those with >3 yr of therapy. Post-HD SBPs of <120 mmHg, however, were associated with increased CV events, thus confirming previous findings of Zager et al.

Other investigators have searched for characteristics that distinguish patients with primary hypertension from those with volume-dependent hypertension so that management of BP in patients with ESRD may be improved (20). In one study, 44-h interdialytic ambulatory pressures, LVM, and inferior vena cava measurements by echocardiography were used for evaluation. In a group of 41 HD patients, withdrawal of antihypertensive medications resulted in sustaining of normal pressures for approximately 1 mo in eight (20%) of the 41 patients. The majority of patients who developed hypertension within a few days had higher ventricular mass indices, had higher average BP values at home, had a faster rate of rise in BPs in the interdialytic period, and were thought more likely to be volume overloaded. That study questioned methods that are used to follow hypertension in the patient with ESRD and suggested that hypervolemia may have a larger role in CV morbidity and mortality rates than previously appreciated. It also supports the notion that the guidance for BP control in patients with ESRD cannot be patterned after the general population, in which lower values are currently favored.

Other studies have examined the role of volume management as a way to optimize BP control in patients who have ESRD and hypertension. Wabel et al. (21) examined the relationship between pre-HD SBP and volume status in 500 dialysis-dependent patients using bioimpedance spectroscopy. Using a hydration reference plot, they examined volume status against relative hydration status (as defined by deviation from a normal volume range in liters [ΔHS]). Using this method, they note that approximately 20% had both normal BPs and ΔHS, while 15% had BPs >140/90 mmHg and a ΔHS >2.5 L. That study, however, did not show definitive trends between volume and magnitude of hypertension: 13% of those with hypertension had ΔHS <1.1 L, and 10% with pre-HD pressures of <140 mmHg had ΔHS >2.5 L (13).

An even more recent approach to assessing the role of volume and BP control came from Agarwal et al. (22), who evaluated the role of aggressive ultrafiltration in HD patients and its affect on BP in the Dry-Weight Reduction in Hypertensive Hemodialysis Patients (DRIP) study. Using a research protocol, 100 patients underwent their normal HD with half of the patients randomly assigned to have an additional amount of fluid removed without extra dialysis time. The primary goal was to improve interdialytic systolic ABPMs averaged over 44 h weekly. The volumes of ultrafiltration were governed by patient report and clinical evidence of hypovolemia (severe hypotension, cramps, and dizziness). They demonstrated that with weight reduction, BP values decreased and were sustained during an 8-wk period without change in antihypertensive regimen or pedal edema (22). They also noted a reduction in pulse pressure among those who maintained lower BP. This confirms previous findings in another large study that examined changes in vascular compliance and outcomes in HD patients (23).

Although these studies do not solve the problem of what the BP level should be, they are consistent in noting that lower BPs are associated with higher CV event rates and that those with wide pulse pressures are at higher CV risk. It is also clear that conventional approaches to measuring BP that are accepted for the general population are not adequate for the ESRD population. Home BP measurements on nondialysis days and 24-h ABPMs seem to provide even more informative data in the group with ESRD (22). Furthermore, home BP measurements can detect changes in ABPMs in a reliable manner (24); therefore, in addition to monitoring for the known CV risk factors as in the general population, patients with ESRD need more aggressive fluid goals to optimize BP goals. Home BP monitoring on interdialytic days is gaining momentum as a way to gain more meaningful information regarding CV risk. Once an accepted method for assessing BP becomes available in the context of volume control, a clinical trial should be commissioned to assess its impact on CV outcomes.

The ESRD population has heart failure admission rates five times higher than those without CKD and has heart disease
admission rates and arrhythmias two times higher than in the general population (3). With the growing prevalence of CKD in the United States and ESRD rates rising, evidence-based guidelines are needed regarding the diagnosis of hypertension and its accurate measurement and management and the effect of medication on overall outcomes. Ambulatory BP readings, volume control, and central aortic pressure measurements all are steps in the right direction. Last, the type of antihypertensive therapy in this subgroup of patients does not seem to be as impactful as in the general population as long as SBP levels are reduced (25).

It is clear from this overview that the paucity of data as to when and how to measure BP optimally in dialysis patients to achieve maximal impact on CV risk reduction is unknown. Randomized trials are obviously needed to obtain clear answers to these questions so that meaningful guidelines can be written.

Disclosures

None.

References


