Ambulatory Blood Pressure in Kidney Transplant Recipients: More Questions than Answers

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Hypertension is an established risk factor for several chronic conditions such as ischemic heart disease, stroke, dementia, and chronic kidney disease (CKD) [1, 2]. It is the most prominent risk factor in kidney transplant recipients (KTRs) with a reported overall prevalence of 67–95%, with increasing prevalence as kidney function declines [3, 4]. Most KTRs have hypertension prior to transplant or develop arterial hypertension after the transplantation. This posttransplant hypertension is one of the major contributors to posttransplant cardiovascular morbidity and mortality. It also contributes to graft damage, resulting in decreased allograft survival, and significantly decreases long-term patient survival [5]. The accurate diagnosis and management of posttransplant hypertension demand attention.

Several methods are available to diagnose and manage posttransplant hypertension and improve long-term patient outcomes in KTRs. These methods are not unique to KTRs and include conventional office blood pressure (BP) measurement and 24-h ABPM. While nearly all of the observational studies and clinical trials that define our understanding of hypertension risk and inform treatment guidelines utilized office BPs, 24-h ABPM is considered as the gold standard of BP measurement. Conventional office BP measurement is the traditional method of measuring BP where the BP of the patient is measured in

an office setting. However, office BP measurements are limited because they are often obtained using techniques that are not guideline adherent and office BP alone does not allow for identification of important BP phenotypes such as white-coat and masked hypertension. White-coat hypertension is defined as having controlled ambulatory BP but elevated clinic BP, whereas masked hypertension is defined as controlled clinic BP but elevated ambulatory BP. White-coat hypertension and masked hypertension are clinically significant; multiple studies have demonstrated masked hypertension, and to a lesser extent white-coat hypertension, is associated with increased risk for target organ damage and cardiovascular events.

Patients with CKD are more likely to be hypertensive due to multiple factors, which also likely contribute to elevated ambulatory BP and increased prevalence of masked and sustained hypertension. The International Database of Ambulatory BP in Renal Patients (I-DARE) group evaluated the prevalence of masked and sustained hypertension in patients with CKD in 5 different cohorts, including the African American Study of Kidney Disease (AASK), the Chronic Renal Insufficiency Cohort (CRIC), the CKD Japan Cohort (CKD-JAC), a Spanish cohort, and an Italian cohort [6]. The prevalence varied between the cohorts. AASK, CRIC, and CKD-JAC reported a high prevalence of both masked (30–35%) and sustained (18–

36%) hypertension, whereas the Italian and Spanish cohorts reported a lower prevalence of masked hypertension (6–10%) but a high prevalence of sustained (41–49%) hypertension.

The methods and optimal office BP threshold to diagnose hypertension in patients with CKD and KTRs are a matter of debate due to differences in various guidelines. In this issue of the *American Journal of Nephrology*, Korogiannou and colleagues conducted a cross-sectional study in a cohort of 205 KTRs to determine the prevalence and rates of treatment and control of hypertension assessed by office BP and ABPM [7]. They utilized 2 different thresholds from the ESH/ESC and ACC/AHA guidelines for office and ambulatory BP to define hypertension. They also identified the proportion of patients with white-coat and masked hypertension. The study reported the hypertension prevalence to be greater when utilizing ABPM than office BPs (94.1% and 98.5% at $\geq 130/80$ mm Hg and $\geq 125/75$ mm Hg ambulatory BP thresholds, respectively, as compared to 88.3% and 92.7% at $\geq 140/90$ mm Hg (ESH/ESC) and $\geq 130/80$ mm Hg (ACC/AHA) office-based definitions, respectively). The control rates were higher in the office setting than ABPM (69.6% and 43.7% with ESH/ESC and ACC/AHA office cutoffs, respectively, compared to 38.3% and 21.3% with ambulatory BP). In these KTRs, white-coat hypertension was diagnosed in 6.7% of patients at 140/90 office and 130/80 ABPM and 5.9% patients at 130/80 office and 125/75 ABPM thresholds. The prevalence of masked hypertension was higher with 39.5% KTRs diagnosed at the 140/90 office and 130/80 ABPM thresholds and 31.7% diagnosed at the 130/80 office and 125/75 ABPM thresholds. The high prevalence of these discordant BP phenotypes is also reflected in a low sensitivity and specificity of office BP for detecting high ambulatory BP. The positive prognostic value of an elevated office BP ranged from 76 to 89%, while the negative prognostic value was only 35–49%.

Prior studies in KTRs found that the prevalence of hypertension varied between 17% and 72% in studies that utilized an office BP threshold of 140/90 mm Hg as compared to 22–95% in studies that used the 130/80 mm Hg threshold. This difference in the prevalence of hypertension in KTRs can be attributed to numerous factors, including differences in study cohorts with regard to the specific kidney donor and recipient factors. On the other hand, the prevalence of hypertension was reported to be ranging between 24% and 95% in studies that used ABPM at the 130/80 mm Hg threshold [8, 9]. Another study by Ahmed et al. [10] evaluated the prevalence of hypertension at both the 130/80 mm Hg office threshold and the

corresponding 125/75 mm Hg ABPM threshold. In that study, hypertension prevalence was estimated at 21.5% with a 130/80 mm Hg office threshold and 77% with a 125/75 mm Hg ABPM threshold.

The poor concordance between office and ambulatory BP with especially high rates of masked hypertension in KTRs and patients with CKD is clinically significant. Observational studies in the general population and in those with CKD have indicated increased risk for cardiovascular and renal outcomes in patients with masked hypertension. Patients with white-coat hypertension are at increased risk for adverse outcomes compared to those with controlled office and ambulatory BP. Despite a lack of clinical trials comparing office-based to out-of-office-based hypertension management, recent guidelines from KDIGO, ACC/AHA, and ESH/ESC recommend out-of-office BP for diagnosis and management of hypertension [11–13]. While there have not been studies comparing office-based to out-of-office-based hypertension treatment, a meta-analysis of randomized controlled trials identified clinically meaningful reductions in both systolic and diastolic BP at 6 months and 1 year with the use of self-monitoring BP as compared to usual care, especially when paired with a team-based approach.

Clinical trials are needed to determine whether treatment based on out-of-office BPs reduces risk for adverse outcomes in patients with white-coat and masked hypertension. These trials are especially important in KTRs and those with CKD given the high rates of masked hypertension in these populations. Additionally, further research to improve the accuracy of in-office BP measurement should be conducted as it could help standardize care and further improve patient outcomes. Hypertension is a significant risk factor for cardiovascular disease and all-cause mortality in KTRs; accurate assessment of BP is key to diagnosing and managing hypertension in order to reduce hypertension-related adverse outcomes in KTRs. The study by Korogiannou and colleagues highlights the need to expand the use of out-of-office BP measurements to identify the significant proportion of KTRs with white-coat and masked hypertension, BP phenotypes that, in the absence of clinical trial data, require a thoughtful approach to management.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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