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Use of ambulatory blood pressure monitoring in kidney transplant recipients

Adrian M. Whelan ^{1,2} and Elaine Ku¹

¹Division of Nephrology, Department of Medicine, University of California, San Francisco, CA, USA and ²Nephrology Section, San Francisco VA Medical Center, San Francisco, CA, USA

Correspondence and offprint requests to: Adrian M. Whelan; E-mail: adrian.whelan@ucsf.edu

In this issue of *NDT* Mallamaci *et al.* [1], report on the results from a cohort study of longitudinal blood pressure (BP) measurements in kidney transplant recipients and compare routinely measured office BPs with 24-h ambulatory BPs (ABPs). The investigators found that white coat hypertension was present in 25% and masked hypertension in 12% of kidney transplant recipients. The authors found generally poor agreement between office BP and ABP readings, with misclassification of BP control status at 37% of visits, where a therapeutic change in BP management may have been indicated. The study focused on

office BPs taken routinely in clinical practice rather than standardized research measurements per protocol. While this may have contributed to the poor agreement between office and ABP readings, it highlights that relying solely on routinely measured BP in the clinic may not provide an accurate evaluation of BP status. Overall, the study adds to a limited evidence base surrounding how to best measure BP and manage hypertension in kidney transplant recipients.

Previous studies using ambulatory blood pressure monitoring (ABPM) in kidney transplant recipients have been

Table 1. Recommended BP targets for CKD and kidney transplant recipients by guideline

Guideline	CKD goal	Kidney transplant-specific goal
ESC/ESH 2018 [20]	Systolic BP 130–139 mmHg	No recommendation
ACC/AHA 2017 [7]	<130/80 mmHg	<130/80 mmHg
JNC 8 2014 [21]	<140/90 mmHg	No recommendation
KDIGO BP in CKD guideline 2012 [9]	≤140/90 mmHg (uAER <30 mg/24 h) ≤130/80 mmHg (uAER >30 mg/24 h)	≤130/80 mmHg
KDIGO kidney transplant recipient guideline 2009 [8]	–	<130/80 mmHg

ACC, American College of Cardiology; AHA, American Heart Association; ESC, European Society of Cardiology; ESH, European Society of Hypertension; JNC, Joint National Committee; KDIGO, Kidney Disease: Improving Global Outcomes; uAER, urine albumin excretion rate per 24 h (or equivalent).

predominantly single center and cross-sectional in design and confirmed that the rates of white coat hypertension and masked hypertension are within the range reported in this study [2–6]. Similar to other prior studies, an office BP $\geq 140/90$ mmHg was used to classify patients as being hypertensive, even though clinical practice guidelines on the management of high BP recommend maintaining BP $\leq 130/80$ mmHg in kidney transplant recipients [7–9]. However, had an office BP of $>130/80$ mmHg been used for the diagnosis of hypertension (with the corresponding lower ABP value of $>125/75$ mmHg for mean 24-h ABP) [7], it is possible that the rate of white coat hypertension and masked hypertension may have differed from the prevalence reported in this study.

It is known that the prevalence of office-based hypertension (when defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg and/or treatment with antihypertensives) in kidney transplant recipients has been reported to be $>80\%$ [10, 11]. This high prevalence is thought to be secondary to a number of factors, including the presence of long-standing hypertension prior to transplantation, the hypertensive side effect of immunosuppression regimens (steroids and calcineurin inhibitors), donor-related factors (including older donor age, preexisting donor hypertension and poor allograft quality), transplant renal artery stenosis and graft rejection, in addition to traditional risk factors [12–15]. Kidney transplant recipients differ fundamentally from the general population in terms of their greater degree of vascular calcification and higher prevalence of diabetes and other comorbidities and should be considered to be at the highest risk for cardiovascular disease. Indeed, cardiovascular disease is the leading cause of death following kidney transplantation, with an annual risk of cardiovascular events of 3.5–5% per year, which is 50-fold higher than that of the general population [16–19]. Aggressive cardiovascular risk factor modification, including appropriate control of BP, is indicated in kidney transplant recipients.

While current clinical practice guidelines include recommendations for the management of hypertension in the context of chronic kidney disease (CKD), only a few guidelines have specific recommendations for the management of hypertension in kidney transplant recipients (Table 1). This is likely reflective of the lack of randomized controlled trials of alternate BP targets assessing renal, cardiovascular or mortality outcomes in the transplant population. The best level of evidence available currently for BP goals in kidney transplant recipients stem from an observational *post hoc* analysis of a large randomized controlled trial of folic acid use in kidney transplant recipients

(Folic Acid for Vascular Outcome Reduction study), which showed a monotonic relationship between higher systolic BP and the risk of cardiovascular disease and all-cause mortality. In contrast, lower diastolic BP (<70 mmHg) was associated with an increased risk of cardiovascular disease and all-cause mortality, but not if diastolic BP was >70 mmHg [22].

ABPM has been thought to play an important role in confirming a new diagnosis of hypertension, ruling out white coat hypertension and detecting masked hypertension, the latter being of particular importance given the strong observational associations with end-organ damage close to or even greater than that of sustained hypertension [23–27]. However, our knowledge of what ABPM parameters are predictive of outcomes specifically in transplant recipients is limited. One study has shown that reverse dipping status (inappropriate rise in BP during the night) is associated with worse allograft survival [28], but determining a causal relationship in these studies is difficult, as deteriorating allograft function may be a cause for changes in BP. Whether and how to incorporate ABPM data from transplant recipients to optimize their outcomes is less clear. Thus, while Mallamaci's *et al.* [1] findings of a substantial prevalence of missed and inadequately treated masked hypertension is important, the amount of focus that should be placed on controlling out-of-office BP in this population remains unclear and the optimal office or out-of-office BP targets remain untested aside from extrapolation of data from the general or CKD population.

Implementing a policy of routine ABPM on all transplant recipients during follow-up, similar to that performed by Mallamaci *et al.* [1], would require significant resources, including the cost of the devices and their routine calibration, human resources to operate the devices and download data and program maintenance (placement and return of devices). In addition, patient compliance and acceptability remain a challenge, as ABPM requires in-person fitting and return of the device, is uncomfortable and disruptive to sleep [29] and can be challenging to repeat during short-term intervals to confirm BP control with therapy titration. There may also be system-level barriers; in the USA, the cost of ABPM performance is only reimbursed by the Centers for Medicare and Medicaid Services for the confirmation of suspected white coat hypertension but not for other indications such as screening for masked hypertension or abnormal diurnal BP patterns. Home BP monitoring may be a logistically more feasible alternative that would facilitate more frequent monitoring of BP, especially with changes to therapy, although nocturnal BP data cannot be easily obtained with this

approach. Furthermore, the proportion of patients with hypertension remained stable over the course of this study despite widespread use of ABP monitors. This suggests that therapeutic inertia or failure of health care providers to initiate or intensify therapy when therapeutic goals are not reached may be a bigger barrier to achieving BP control in the transplant recipient population than a limited availability of ABP readings [30].

Overall, significant evidence gaps regarding the optimal approach to BP management in kidney transplant recipients remain. We have limited evidence to guide how best to detect and monitor BP in our transplant recipients and a trial to determine the optimal BP target that improves cardiovascular and renal outcomes as well as mortality is needed. The inclusion of kidney transplant recipients in clinical BP trials may also help address the evidence gaps. Providing answers to these issues is particularly important in the kidney transplant population, which remains at substantial cardiovascular risk even when renal function is restored with transplantation.

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CONFLICT OF INTEREST STATEMENT

None declared.

(See related article by Mallamaci *et al.* Long-term blood pressure monitoring by office and 24-h ambulatory blood pressure in renal transplant patients: a longitudinal study. *Nephrol Dial Transplant* 2019; 34: 1558–1564)

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