Original Article

KIDNEY RESEARCH AND CLINICAL PRACTICE

Ambulatory blood pressure trajectories and blood pressure variability in kidney transplant recipients: a comparative study against chronic kidney disease patients

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Background: Hypertension is a major cardiovascular risk factor in both kidney transplant recipients (KTRs) and patients with chronic kidney disease (CKD). Ambulatory blood pressure monitoring (ABPM) is considered the gold-standard method for hypertension management in these subjects. This is the first study evaluating the full ambulatory blood pressure (BP) profile and short-term BP variability (BPV) in KTRs versus CKD patients without kidney replacement therapy.

Methods: Ninety-three KTRs were matched with 93 CKD patients for age, sex, and estimated glomerular filtration rate. All participants underwent 24-hour ABPM. Mean ambulatory BP levels, BP trajectories, and BPV indices (standard deviation [SD], weighted SD, and average real variability) were compared between the two groups.

Results: There were no significant between-group differences in 24-hour systolic BP (SBP)/diastolic BP (DBP) (KTRs: 126.9 ± 13.1/79.1 ± 7.9 mmHg vs. CKD: 128.1 ± 11.2/77.9 ± 8.1 mmHg, p = 0.52/0.29), daytime SBP/DBP and nighttime SBP; nighttime DBP was slightly higher in KTRs (KTRs: 76.5 ± 8.8 mmHg vs. CKD: 73.8 ± 8.8 mmHg, p = 0.04). Repeated measurements analysis of variance showed a significant effect of time on both ambulatory SBP and DBP (SBP: F = [19, 3002] = 11.735, p < 0.001, partial η^2 = 0.069) but not of KTR/CKD status (SBP: F = [1, 158] = 0.668, p = 0.42, partial η^2 = 0.004). Ambulatory systolic/diastolic BPV indices were not different between KTRs and CKD patients, except for 24-hour DBP SD that was slightly higher in the latter group (KTRs: 10.2 ± 2.2 mmHg vs. CKD: 10.9 ± 2.6 mmHg, p = 0.04). No differences were noted in dipping pattern between the two groups.

Conclusion: Mean ambulatory BP levels, BP trajectories, and short-term BPV indices are not significantly different between KTRs and CKD patients, suggesting that KTRs have a similar ambulatory BP profile compared to CKD patients without kidney replacement therapy.

Keywords: Ambulatory blood pressure monitoring, Blood pressure variability, Chronic kidney diseases, Hypertension, Kidney transplantation

Introduction

Hypertension is a major risk factor for cardiovascular disease, renal function decline, and all-cause mortality in patients with chronic kidney disease (CKD), and its prevalence gradually increases alongside advancing CKD stages [1]. Ambulatory blood pressure monitoring (ABPM) is considered the gold-standard method for hypertension diagnosis and management in patients with CKD [2–5] due to several advantages, including high prognostic value for future adverse events [6,7], the identification of different hypertension phenotypes (i.e., white coat and masked hypertension), [6,7] and, finally, the ability to capture short-term blood pressure variability (BPV), which is also an independent risk factor for cardiovascular events and mortality in CKD patients [8].

Kidney transplantation is considered the optimal treatment option for patients with kidney failure, as it greatly improves cardiovascular morbidity and mortality compared to both hemodialysis and peritoneal dialysis treatment [9]. Despite the significant reductions in cardiovascular risk, kidney transplant recipients (KTRs) still have a higher risk of future cardiovascular events and death compared to the general population [10]. The high prevalence of hypertension in this population (70%–90%) [11] is considered a major factor involved in these associations [9,11,12]. Of note, "masked" hypertension, a hypertension phenotype particularly associated with higher risk of cardiovascular disease, renal disease, and death [13], is also highly prevalent in KTRs [14].

Although the role of ABPM in CKD and kidney transplantation has been highlighted in recent consensus documents [4,12], as of this writing, there are only scarce data comparing ambulatory blood pressure (BP) levels between KTRs and CKD patients without kidney replacement therapy. In the only relevant study [14], KTRs had significantly higher ambulatory systolic BP (SBP) levels than individuals with CKD, whereas there were no differences between these two groups in office BP levels; this study, however, only examined average BP levels and not full ambulatory BP trajectories during a typical 24-hour period or short-term BPV. Thus, the aim of the present study was to evaluate for the first time the full ambulatory BP profile, as well as the indices of short-term BPV, in KTRs in comparison to CKD patients without kidney replacement therapy.

Methods

Study participants

This is an observational study that includes matched cases and controls. We recruited KTRs from the renal transplantation outpatient clinic of the Department of Nephrology, Laiko General Hospital in Athens and patients with CKD from the outpatient clinic of the Department of Nephrology, Hippokration Hospital in Thessaloniki, Greece. Adult patients that received a kidney transplant at least 3 months prior to study recruitment were included as cases; a blinded member of our group matched KTRs with potential controls from a large cohort of stage 1–4 CKD patients at a 1:1 ratio on the basis of age, sex, and estimated glomerular filtration rate (eGFR; calculated with the CKD-Epidemiology Collaboration formula) (Supplementary Fig. 1, Supplementary Table 1; available online). Inclusion and exclusion criteria for the two study groups are presented in Supplementary Table 2 (available online). All evaluations were performed according to the Declaration of Helsinki (2013 Amendment); all participants provided informed written consent prior to participation. The study protocol was approved by the Ethics Committee of the Aristotle University of Thessaloniki School of Medicine and by the Data Protection Management of Laiko General Hospital of Athens (No. 8052/15-06-2017).

Data collection and study measurements

Study subjects were evaluated during a scheduled visit at the relevant clinic. Demographics, anthropometric characteristics, comorbidities, concomitant medication, and other CKD-related information were collected for each participant. A physical examination and venous blood sampling for routine hematological and biochemical tests were also performed. Office BP readings were performed at the level of the brachial artery according to the relevant guidelines [3]. All captured information was transferred in a purpose-built electronic datasheet.

In both KTRs and CKD patients, ABPM was performed with the Mobil-O-Graph device (IEM, Stolberg, Germany), a validated oscillometric device [15,16] whose brachial BP-detection unit was validated according to standard protocols and was shown to provide practically identical val-

ues with a widely used ABPM monitor, Spacelabs 90217A (Spacelabs Medical, Inc., Snoqualmie, WA, USA) [17]. ABPM was performed with a cuff of appropriate size for 24 hours as described previously [18,19]. The ABPM device was placed on the opposite arm for KTRs with a functioning arteriovenous fistula. All participants were instructed to continue their regular medication and follow their usual activities. Measurements were included in analysis if >70% of recordings were valid with ≤2 non-consecutive day-hours with <2 valid measurements and ≤1 night-hour without valid recording for each 24-hour period [20]. In order to minimize the possible effect of manual BP measurements, only measurements recorded at the prespecified time intervals at which the device was set to take measurements were used in this analysis.

Furthermore, based on ABPM recordings, BPV indices of brachial SBP and diastolic BP (DBP) (standard deviation [SD], weighted SD, and average real variability) were calculated from validated formulas as described previously (Supplementary Table 3, available online) [18,21]. The dipping pattern of nocturnal BP was calculated with the following formula: 1 – mean night/mean day ratio of SBP (%). Patients were divided into the following groups: extreme dippers (nocturnal BP fall of >20%), dippers (fall of >10% and ≤20%), non-dippers (fall of ≥0% and ≤10%), and reverse dippers (nocturnal increase in SBP).

Statistical analysis

The Kolmogorov-Smirnov test was applied to examine the normality of distribution for quantitative variables. Continuous variables are expressed as mean ± SD or as median (interquartile range) according to the normality of the distribution. Categorical variables are presented as absolute frequencies and percentages (n, %). Between-group comparisons for continuous variables were performed with the independent t test or the Mann-Whitney test, where applicable; categorical variables were compared with the chi-square test or the Fisher exact test. To evaluate the effect of group (KTRs vs. CKD patients) and time on the trends of ambulatory BP levels and to determine whether an interaction between the two existed, we compared the mean hourly values of SBP and DBP between KTRs and CKD patients using two-way mixed analysis of variance (ANOVA) for repeated measurements for a 20-hour period

(12:00 PM to 8:00 AM), during which, data were available for all participants following different starting time of the ABPMs. The Greenhouse-Geiser correction was applied to overcome the violation of the sphericity assumption. Moreover, time profiles of BP levels were investigated using linear mixed models (LMM) procedure to create estimates of BP and their association with KTR/CKD status and other covariates during a 24-hour ABPM. A random intercept and random slope model was utilized, and an unstructured covariance structure provided the best fit of the data based on Akaike information criterion and Schwarz's Bayesian information criterion values after testing other covariance matrices. The p-values of <0.05 (two-tailed) were considered statistically significant for all comparisons. Statistical analysis was performed with IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

Results

Demographic and clinical characteristics of kidney transplant recipients and chronic kidney disease patients

Demographic characteristics, comorbidities, concomitant medication use, and main laboratory data of the two study groups (93 KTRs and 93 CKD patients) are presented in Table 1. As expected, the two groups were not different in terms of age (KTRs: 61.3 ± 9.6 years vs. CKD: 63.8 ± 9.9 years, p = 0.09), sex distribution (KTRs: 32.3% females vs. CKD: 32.3% females, p = 1.00) or eGFR (KTRs: 60.2 ± 22.1 mL/min/1.73 m^2 vs. CKD: 60.6 ± 24.3 mL/min/1.73 m^2, p = 0.92). In addition, there were no differences between the two groups regarding all major comorbidities except for diabetes (KTRs: 36.6% vs. CKD: 54.8%, p = 0.01) and smoking (KTRs: 9.7% vs. CKD: 23.7%, p = 0.01), which were less common in KTRs. Among KTRs, 80.6% were receiving tacrolimus, 91.4% were receiving mycophenolate mofetil/mycophenolic acid, and 76.3% were administered corticosteroids for immunosuppression.

KTRs and CKD patients had similar office SBP levels (KTRs: 130.8 ± 17.2 mmHg vs. CKD: 129.9 ± 9.3 mmHg, p = 0.64); however, office DBP was significantly lower in KTRs (KTRs: 74.5 ± 10.8 mmHg vs. CKD: 81.1 ± 7.6 mmHg, p < 0.001). The number of prescribed antihypertensive drugs was slightly but not significantly higher in CKD patients (KTRs: 2.0 ± 1.2 vs. CKD: 2.3 ± 1.4, p = 0.06); the use of angio-

Table 1. Demographic, anthropometric, and clinical characteristics of the study participants

Characteristic	KTR group	CKD group	p-value
No. of patients	93	93	
Age (yr)	61.3 ± 9.6	63.8 ± 9.9	0.09
Female sex	30 (32.3)	30 (32.3)	1.00
Time since the initiation of RRT (mo)	161 [103.2]	-	-
Time since kidney transplantation (mo)	90.3 [128.4]	-	-
Body mass index (kg/m^2)	27.7 ± 16.9	30.4 ± 6.0	0.14
Hypertension	85 (91.4)	83 (89.2)	0.62
Diabetes	34 (36.6)	51 (54.8)	0.01*
Dyslipidemia	59 (63.4)	61 (65.6)	0.65
Cardiovascular disease	18 (19.4)	25 (26.9)	0.22
Coronary heart disease	15 (16.1)	12 (12.9)	0.53
Stroke	2 (2.2)	4 (4.3)	0.68
Peripheral arterial disease	4 (4.3)	10 (10.8)	0.01*
Smoking	9 (9.7)	22 (23.7)	0.01*
Office SBP (mmHg)	130.8 ± 17.2	129.9 ± 9.3	0.64
Office DBP (mmHg)	74.5 ± 10.8	81.1 ± 7.6	<0.001*
No. of antihypertensive drugs	2.0 ± 1.2	2.3 ± 1.4	0.06
ACEi/ARBs	44 (47.3)	59 (67.3)	0.03*
Calcium-channel blockers	43 (46.2)	50 (53.8)	0.31
MRAs	0 (0.0)	2 (2.2)	0.497
Beta-blockers	64 (68.8)	44 (47.3)	0.003*
Alpha-blockers	2 (2.2)	13 (14.0)	0.003*
Nitrates	2 (2.2)	1 (1.1)	1.00
Central acting agents	12 (12.9)	8 (8.6)	0.34
Diuretics	17 (18.3)	42 (45.2)	<0.001*
Statins	41 (44.1)	59 (63.4)	0.008*
Immunosuppressive drugs			
Cyclosporine	13 (14.0)		
Tacrolimus	75 (80.6)		
mTORi	11 (11.8)		
MMF/MPA	85 (91.4)		
Azathioprine	1 (1.1)		
Corticosteroids	71 (76.3)		
Hemoglobin (g/dL)	13.1 ± 1.6	13.7 ± 1.5	0.005*
eGFR CKD-EPI (mL/min/1.73 m^2)	60.2 ± 22.1	60.6 ± 24.3	0.92
Creatinine (mg/dL)	1.3 ± 0.5	1.4 ± 0.6	0.63
Urea (mg/dL)	60.1 ± 32.2	53.9 ± 29.6	0.17
Uric acid (mg/dL)	6.4 ± 1.4	6.5 ± 1.4	0.94
Sodium (mEq/L)	140.5 ± 3.2	138.9 ± 2.5	<0.001*
Potassium (mEq/L)	4.5 ± 0.5	4.7 ± 0.4	0.88
Calcium (mg/dL)	9.4 ± 0.6	9.4 ± 0.6	0.001*
Phosphorus (mg/dL)	3.1 ± 0.7	3.5 ± 0.6	0.07
Parathyroid hormone (pg/mL)	66.9 (53.6–113.5)	51.5 (37.2–73.5)	0.02*
C-reactive protein (mg/dL)	3.0 (1.6–3.6)	1.3 (0.8–3.4)	0.001*
Total cholesterol (mg/dL)	188.3 ± 31.9	163.9 ± 38.5	<0.001*
Triglycerides (mg/dL)	149.4 ± 62.6	158.0 ± 92.2	0.46

Data are expressed as number only, mean ± standard deviation, or number (%), or median (interquartile range).

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; CKD-EPI, CKD-Epidemiology Collaboration; CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; KTR, kidney transplant recipient; MMF, mycophenolate mofetil; MPA, mycophenolic acid; MRA, mineralocorticoid receptor antagonist; mTORi, mammalian target of rapamycin inhibitors; RRT, renal replacement therapy; SBP, systolic blood pressure.

*p < 0.05 is statistically significant.

tensin-converting enzyme inhibitor/angiotensin II receptor blockers (KTRs: 47.3% vs. CKD: 67.3%, p = 0.03), α-blockers (KTRs: 2.2% vs. CKD: 14.0%, p = 0.003) and diuretics (KTRs: 18.3% vs. CKD: 45.2%, p < 0.001) was less frequent while the use of β-blockers was more frequent in KTRs compared to CKD patients (KTRs: 68.8% vs. CKD: 47.3%, p = 0.003).

Comparison of ambulatory blood pressure levels between kidney transplant recipients and chronic kidney disease patients

Table 2 presents the mean ambulatory values for SBP, DBP, and pulse pressure (PP) in KTRs and CKD patients. As noted in the table, there were no significant differences between the two groups in the 24-hour SBP (KTRs: 126.9 ± 13.1 mmHg vs. CKD: 128.1 ± 11.2 mmHg, p = 0.52) and DBP (KTRs: 79.1 ± 7.9 mmHg vs. CKD: 77.9 ± 8.1 mmHg, p = 0.29). This was also the case for daytime and nighttime BP levels, with the exception of nighttime DBP, which was higher in KTRs compared to CKD patients (KTRs: 76.5 ± 8.8 mmHg vs. CKD: 73.8 ± 8.8 mmHg, p = 0.04). PP levels were similar between KTRs and CKD patients over all periods studied.

White coat and masked hypertension in kidney transplant recipients and chronic kidney disease patients

Fig. 1 illustrates the prevalence of different BP phenotypes among the two study groups. The prevalence of white coat hypertension was similar between the two groups, and the prevalence of masked hypertension may have been higher in KTRs than CKD patients, though not statistically significant (24.7% vs. 16.1%, p = 0.15).

Trajectories of ambulatory blood pressure in kidney transplant recipients and chronic kidney disease patients

The trajectories of hourly mean SBP and DBP levels estimated using two-way mixed ANOVA for repeated measurements in patients with CKD and in KTRs are depicted in Fig. 2. Visual inspection of the figures reveals similar patterns in ambulatory BP between the two groups. After an initial decline in SBP levels during the afternoon, a gradual rise was evident during the evening hours, succeeded by a nocturnal fall and, finally, a morning BP surge in both groups. A similar pattern was noted for ambulatory DBP.

With regards to SBP levels, a significant effect of time (F = [19, 3002] = 11.735, p < 0.001, partial η^2 = 0.069) but not of CKD/KTR status (F = [1, 158] = 0.668, p = 0.42, partial η^2 = 0.004) was noted. There was no significant interaction between time and status on SBP levels over the examined pe-

Table 2. Ambulatory BP levels during the 24-hour, daytime and nighttime period in KTR group and CKD group

Variable	KTR group (n = 93)	CKD group (n = 93)	p-value
Systolic BP (mmHg)			
24-Hour	126.9 ± 13.1	128.1 ± 11.2	0.52
Daytime	127.2 ± 12.9	129.5 ± 11.5	0.20
Nighttime	125.9 ± 16.5	124.6 ± 13.7	0.57
Diastolic BP (mmHg)			
24-Hour	79.1 ± 7.9	77.9 ± 8.1	0.29
Daytime	79.8 ± 8.1	79.5 ± 8.6	0.81
Nighttime	76.5 ± 8.8	73.8 ± 8.8	0.04*
Pulse pressure (mmHg)			
24-Hour	47.8 ± 9.7	50.2 ± 9.6	0.10
Daytime	47.4 ± 9.6	50.1 ± 9.8	0.06
Nighttime	49.4 ± 11.5	50.8 ± 10.1	0.38

Data are expressed as mean ± standard deviation.
BP, blood pressure; CKD, chronic kidney disease; KTR, kidney transplant recipient.
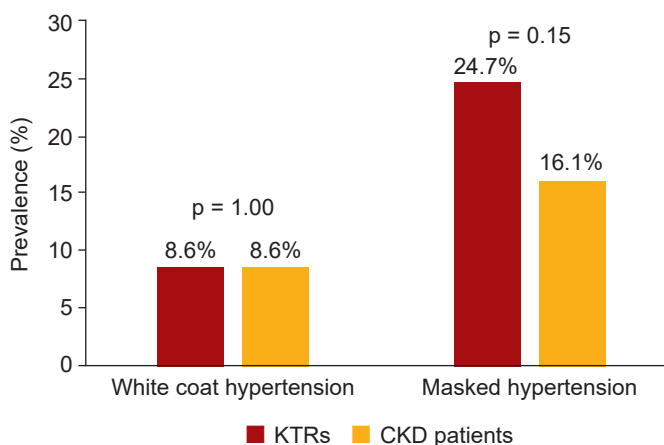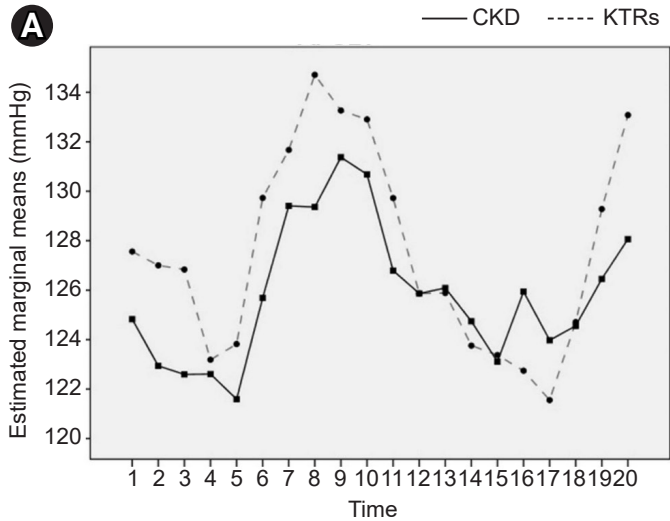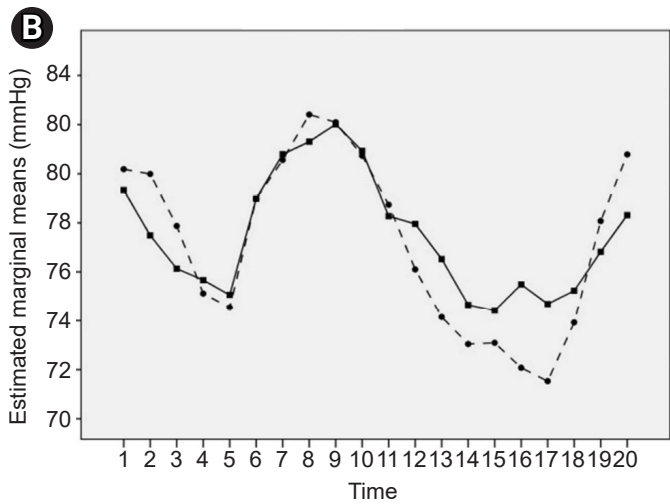*p < 0.05 is statistically significant.

Figure 1. Prevalence of white coat and masked hypertension in KTRs and CKD patients.
CKD, chronic kidney disease; KTR, kidney transplant recipient.

Main effect of status: F(l, 158) = 0.668, p = 0.415, partial η^2 = 0.004
Main effect of time: F(19, 3002) = 11.735, p < 0.001, partial η^2 = 0.069
Interaction of time with status: F(19, 3002) = 1.549, p = 0.122, partial η^2 = 0.010

Main effect of status: F(l, 158) = 0.052, p = 0.819, partial η^2 < 0.001
Main effect of time: F(19, 3002) = 18.930, p < 0.001, partial η^2 = 0.107
Interaction of time with status: F(19, 3002) = 1.614, p = 0.087, partial η^2 = 0.010

Figure 2. Trajectories of the hourly mean (A) SBP levels and (B) DBP levels in KTRs and CKD patients.
CKD, chronic kidney disease; DBP, diastolic blood pressure; KTR, kidney transplant recipient; SBP, systolic blood pressure.

riod (F = [19, 3002] = 1.549, p = 0.12, partial η^2 = 0.010). With regards to DBP, there was again a significant effect of time (F = [19, 3002] = 18.930, p < 0.001, partial η^2 = 0.107) but not of CKD/KTR status (F = [1, 158] = 0.052, p = 0.82, partial η^2 < 0.001) and similarly no significant interaction between time and status was found (F = [19, 3002] = 1.614, p = 0.09,

Table 3. Short-term BP variability indices in KTR group compared to CKD group

24-Hour BP (mmHg)	KTR group (n = 93)	CKD group (n = 93)	p-value
Systolic BP			
SD	14.0 ± 3.9	14.6 ± 4.0	0.35
wSD	13.0 ± 3.5	13.7 ± 3.8	0.24
ARV	10.2 ± 2.5	10.4 ± 2.7	0.46
Diastolic BP			
SD	10.2 ± 2.2	10.9 ± 2.6	0.04*
wSD	9.6 ± 2.1	10.2 ± 2.4	0.08
ARV	7.6 ± 1.7	8.1 ± 2.2	0.07

Data are expressed as mean ± standard deviation.
ARV, average real variability; BP, blood pressure; CKD, chronic kidney disease; KTRs, kidney transplant recipients; SD, standard deviation; wSD, weighted SD.
*p < 0.05 is statistically significant.

partial η^2 = 0.010).

Supplementary Table 4 (available online) presents the results of the LMM analysis. Similarly, no significant effect of KTR status on BP levels was found over time. Male sex was statistically significantly associated with a 5.58 mmHg increase in BP (p < 0.001) after adjustment for other covariates. This effect was greater than the effect observed for history of cardiovascular disease. Diabetes and smoking status did not appear to have a significant effect on BP trajectories.

Blood pressure variability indices in kidney transplant recipients and chronic kidney disease patients

BPV indices of 24-hour ambulatory BP recordings in KTRs and CKD patients are presented in Table 3. As shown in the table, all BPV indexes in KTRs were numerically lower but not significantly different than those in CKD patients. However, 24-hour DBP SD was significantly lower in KTRs compared to CKD patients (10.2 ± 2.2 mmHg vs. 10.9 ± 2.6 mmHg, respectively; p = 0.04).

Dipping pattern

Table 4 presents the dipping profiles of the participants during the 24-hour period. The distribution of dipping profiles was not different between the two KTRs and CKD patients.

Table 4. Dipping patterns of SBP values during 24-hour ABPM in KTR group compared to CKD group

24-Hour SBP	KTR group (n = 93)	CKD group (n = 93)	p-value
2-Type classification			0.232
Non-dippers	81 (87.1)	75 (80.6)	
Dippers	12 (12.9)	18 (19.4)	
4-Type classification			0.333
Reverse dippers	34 (36.6)	26 (27.9)	
Non-dippers	47 (50.5)	49 (52.7)	
Dippers	12 (12.9)	18 (19.4)	
Extreme dippers	0 (0)	0 (0)	

Data are expressed as number (%).
ABPM, ambulatory blood pressure monitoring; CKD, chronic kidney disease; KTR, kidney transplant recipient; SBP, systolic blood pressure.

Discussion

The present study is the first to compare BP profile and short-term BPV indices between KTRs and CKD patients without kidney replacement therapy. We found that the mean ambulatory BP levels were not significantly different between the two groups, except for nighttime DBP, which was significantly higher by 2.7 mmHg in the KTR group. Two-way ANOVA for repeated measurements showed a significant effect of time on ambulatory BP, but not a significant effect of group, nor a significant interaction between them. With regards to short-term BPV, all indices studied were not different between the two groups, except for DBP SD, which was higher in CKD patients. The dipping profile was similar between KTRs and CKD patients.

Previous studies in the general population, as well as in CKD patients, suggested that BP differs when measured in the office versus in out-of-office settings; ABPM is considered to be superior to office BP measurements for the prediction of target organ damage, cardiovascular events, and mortality [7]. Furthermore, out-of-office readings provide additional prognostic information, as they lead to the detection of different BP phenotypes (i.e., white coat and masked hypertension), which are also associated with an increased risk of cardiovascular disease [7]. In line with the above evidence in CKD patients, a recent meta-analysis showed that ambulatory BP was more strongly correlated than office BP with markers of target organ damage and vascular dysfunction, whereas ambulatory BP was a stronger predictor of renal function decline in KTRs [22].

To the best of our knowledge, studies comparing mean ambulatory BP values between KTRs and CKD patients (including both CKD patients without kidney replacement therapy and individuals undergoing hemodialysis) are scarce. A few studies comparing KTRs and hemodialysis patients with ABPM showed that both groups generally display similar BP levels [23,24]; however, in a recent study by our group, which is currently the largest in the field, SBP and PP levels were significantly lower in KTRs compared to hemodialysis patients, and BP trajectories differed accordingly [25]. With regards to CKD patients without kidney replacement therapy, in the only study to date comparing the mean ambulatory BP values between 92 KTRs and 97 CKD patients, 24-hour SBP, as well as awake and sleep SBP were significantly higher in KTRs, while office BP was not [14]. In contrast with the aforementioned findings from Azancot et al. [14], in this study, we observed no significant differences in ambulatory BP levels between KTRs and CKD patients, except for nighttime DBP being slightly higher in the former group. The observed differences in nighttime BP could be meaningful and associated with adverse outcomes, as nighttime BP is strongly associated with GFR loss over time, as well as with markers of vascular health, such as carotid-intimal media thickness [26]. Reduced arterial stiffness observed in KTRs compared to CKD patients without kidney replacement therapy could be a prominent factor for the higher DBP levels observed in KTRs [27].

The differences between our findings and those of Azancot et al. [14] may be due to several reasons. First, there is a time difference of about 7 years in the conduction of the studies; as considerable emphasis on hypertension and its consequences in KTRs has been given in recent years [11], better control rates could have been achieved in organized transplantation centers. This is further supported by the fact that the mean number of antihypertensive agents used in our KTR cohort was considerably higher than that of the previous study (2.0 ± 1.2 vs. 1.6 ± 1.3, respectively) [14]. Furthermore, in the present study we employed a careful matching between KTRs and CKD patients on the basis of sex, age, and eGFR levels. This may have provided a more objective picture, as all of these factors are known to impact ambulatory BP levels [1,28].

BPV is known to be independently associated with target organ damage as well as cardiovascular events and mortality in both the general population and CKD patients [6]. In

a cross-sectional study in 16,546 patients with CKD, short-term SBP variability increased with advancing CKD stages, and this increase in BPV was suggested to be involved in the progressive elevation of cardiovascular risk with kidney disease progression [29]. However, there are only a few works investigating BPV in KTRs. Ozkayar et al. [30] have previously shown that KTRs with endothelial dysfunction have significantly higher BPV compared to those without endothelial dysfunction. In a recent case-control study of our group in 204 KTRs and 102 matched for age and sex hemodialysis patients, we showed that KTRs have significantly lower short-term BPV compared to their hemodialysis counterparts [25]. This is the first study to compare short-term BPV between KTRs and CKD patients without kidney replacement therapy, showing no significant differences between the two study groups in all indices studied except for DBP SD. Based on these observations and previous findings that KTRs have significantly lower BPV compared with hemodialysis individuals [25], one could hypothesize that BPV levels are improved after kidney transplantation to a level comparable to that of CKD patients without kidney replacement therapy with similar eGFR. Possible explanations for this improvement include BP lowering and downregulation of sympathetic nervous system overdrive observed after kidney transplantation [31]. Future studies are warranted to delineate the exact mechanisms of this BPV improvement.

Among the strengths of this study are the careful design, elaborating a blinded matching for a set of crucial parameters (i.e., age, sex, and eGFR), and complex analysis using two-way ANOVA for repeated measurements to evaluate the effects of time and patient group on BP levels. In addition, this is the first study assessing short-term BPV in KTRs, including modern and valid indices and not only the SD and coefficient of variation that are highly influenced by the mean and the weight of BP fall during nighttime [18]. The main limitation of our study is its observational nature, which precludes drawing conclusions about potential associations between ambulatory BP and longitudinal outcomes. Future studies are encouraged to delineate these associations. In addition, the matching variables included three different parameters (age, sex, and eGFR), limiting the ability to control for other potential confounders. Finally, we examined a single cohort including only Caucasian patients; thus, further studies are needed to investigate the reproducibility of our findings in other ethnic groups.

In conclusion, this study showed that the mean ambulatory BP levels were not significantly different between KTRs and age-, sex- and eGFR-matched CKD patients, except for nighttime DBP, which was found to be slightly higher in KTRs. Similarly, the ambulatory BP trajectories revealed a similar pattern in the two groups. BPV indices, as well as dipping profiles, were also not different between KTRs and CKD patients. The above results suggest that, in contrast to previous observations, KTRs have a similar ambulatory BP profile compared to CKD patients without kidney replacement therapy. Future studies are needed to examine longitudinal associations of office and ambulatory BP with hard renal and cardiovascular outcomes in KTRs in order to fully define the hypertension-associated risks and the optimal targets for treatment in this population.

Conflicts of interest

All authors have no conflicts of interest to declare.

Authors' contributions

Conceptualization: PS, SM
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