Clinical Kidney Journal, 2022, vol. 15, no. 11, 2097–2106

https://doi.org/10.1093/ckj/sfac162
Advance Access Publication Date: 1 July 2022
Original Article

ORIGINAL ARTICLE

A parallel evaluation of short- and mid-term changes of ambulatory blood pressure in kidney transplant recipients and kidney donors

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ABSTRACT

Introduction. Kidney transplantation (KTx) is associated with improved blood pressure (BP) levels for kidney transplant recipients (KTRs) without evoking significant changes in donors. However, there is a paucity of studies offering simultaneous detailed evaluation of BP profiles over time in transplant donor–recipient pairs. The aim of the present study was the parallel evaluation of ambulatory BP levels and trajectories in KTRs and their respective living kidney donors in the short and mid-term following KTx.

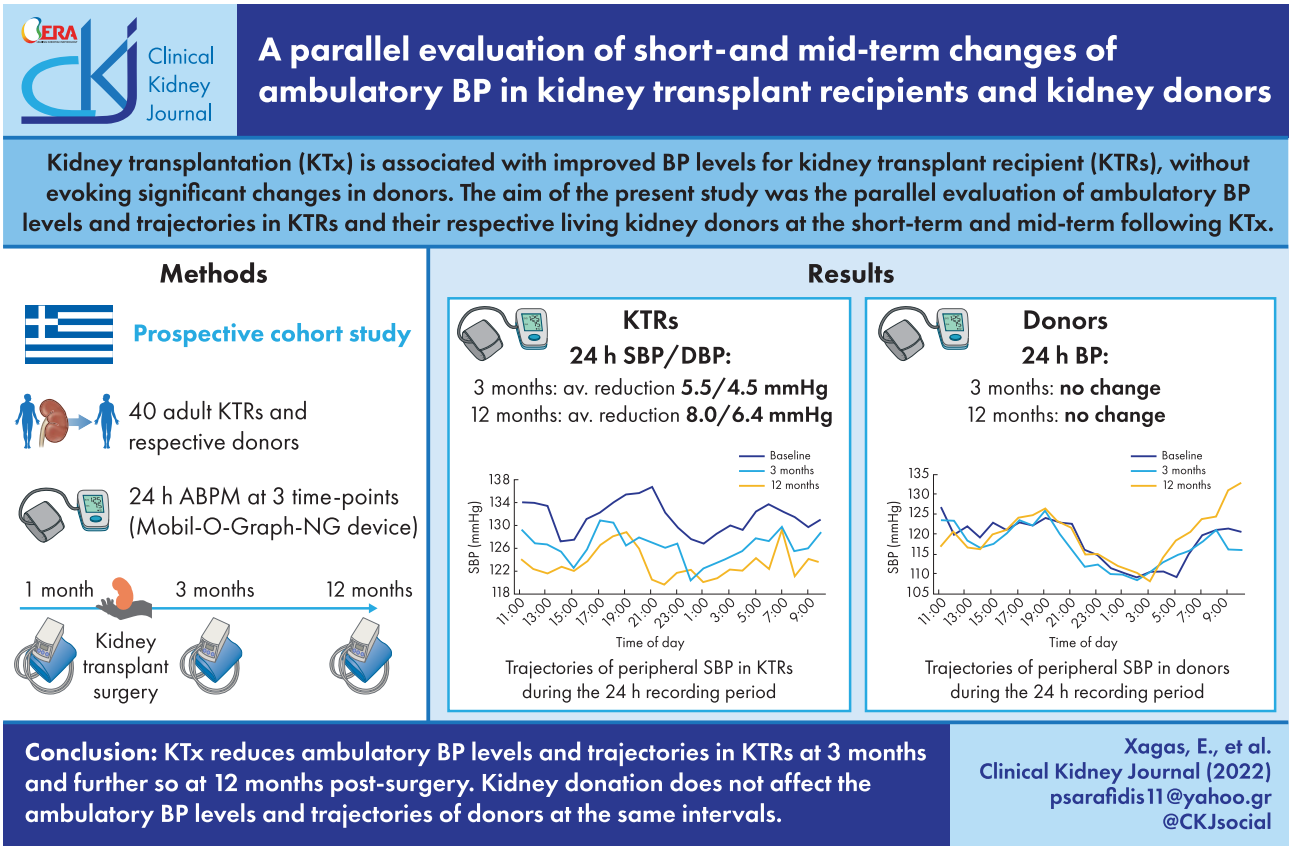
Methods. The study enrolled 40 prospective adult KTRs and their 40 respective donors. All participants were evaluated with 24-h ambulatory BP monitoring (Mobil-O-Graph NG device) at three time points: baseline (1 month before KTx), 3 months and 12 months after KTx.

Results. In KTRs, 3-month 24-h systolic BP (SBP) was marginally reduced and 12-month 24-h SBP significantly reduced compared with baseline [131.9 ± 13.3 versus 126.4 ± 11.9 mmHg ($P = .075$) and 123.9 ± 10.3 mmHg ($P = .009$), respectively]. At both the 3- and 12-month time points, 24-h diastolic BP (DBP) was significantly reduced [86.7 ± 11.5 versus 82.2 ± 8.1 mmHg ($P = .043$) and 80.3 ± 8.5 mmHg ($P = .009$)]. Similar observations were made for day- and night time SBP and DBP. Repeated-measures analysis of variance (ANOVA) showed a significant gradual decrease over time in mean 24-h SBP [$F(1.463, 39.505) = 3.616$; $P = .049$, partial $\eta^2 = 0.118$] and DBP [$F(1.374, 37.089) = 11.34$; $P = .055$, partial $\eta^2 = 0.116$]. In contrast, in kidney donors, 24-h SBP [118.5 ± 11.6 versus 118.2 ± 12.8 mmHg ($P = .626$) and 119.2 ± 11.4 mmHg ($P = .748$)] and DBP did not change at 3 or 12 months compared with baseline; repeated measures ANOVA showed no differences in the mean 24-h SBP and DBP levels over time. The number of antihypertensive agents decreas in KTRs and remained stable in donors.

Conclusions. KTx reduces ambulatory BP levels and trajectories in KTRs at 3 months and further so at 12 months post-surgery. Kidney donation does not affect the ambulatory BP levels and trajectories of donors at the same intervals.

Received: 11.3.2022; Editorial decision: 1.6.2022

GRAPHICAL ABSTRACT



Keywords: ambulatory BP, kidney transplantation, kidney transplant recipients, living kidney donors, office BP

INTRODUCTION

Kidney transplantation (KTx) is the preferred treatment for patients with end-stage kidney disease (ESKD), as it is associated with improved survival and quality of life compared with dialysis [1, 2]. In recent decades, the survival of kidney transplant recipients (KTRs) has further improved; however, the risk of cardiovascular death in transplanted patients remains significantly higher compared with the general population and cardiovascular disease (CVD) remains the leading cause of death [3, 4].

Hypertension is the most common comorbidity in patients with early or advanced pre-dialysis chronic kidney disease (CKD) [5, 6] as well as in patients with ESKD [7, 8]. In addition, hypertension is the most prominent risk factor in KTRs due to its high prevalence [9] and its strong associations with target-organ damage and poor graft and patient survival [10, 11]. The diagnosis and management of hypertension in KTRs was traditionally based on blood pressure (BP) measurements in the office setting. However, office BP has several limitations in the diagnosis and management of hypertension compared with the gold standard of BP measurement, 24-h ambulatory BP monitoring (ABPM) [12, 13], thus recent guidelines and consensus documents highlight the need of more extended ABPM use in KTRs [5, 14].

KTx from a living donor is the best treatment option for patients with ESKD. Several studies have proven its superiority even when compared with transplantation from a deceased donor for both short- and long-term patient and graft survival [15].

Since the safety of the living donor is of paramount importance, accurate assessment of the presence of hypertension is central to the pretransplant evaluation of any prospective living donor. The 2017 KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors recommends the use of 24-h ABPM in all cases where history or clinical measurements raise doubts whether the prospective donor is hypertensive [16]. Following kidney donation, guidelines recommend lifelong monitoring in an organized donor outpatient clinic that includes adequate monitoring of BP and treatment of hypertension to ensure the overall health and the preservation of renal function of the donor [16].

Current literature suggests that KTx is associated with improved BP levels in transplant recipients compared with the pre-transplant condition [17, 18] or patients on dialysis [19]. In addition, BP levels in kidney donors do not appear to change significantly after renal transplantation [20–23]. To the best of our knowledge, only one previous study evaluated simultaneously the natural course of BP in pairs of kidney recipients and their counterpart kidney donors with ABPM [17]. However, this study included only one post-transplant evaluation and used only mean 24-h BP levels and not the full ambulatory BP profile. Thus the aim of the present study was to evaluate in parallel ambulatory BP levels and trajectories, as well as day- and night-time

BP, in KTRs undergoing living donor KTx and their respective donors in the short- and mid-term follow-up after KTx.

MATERIALS AND METHODS

Study population

This prospective cohort study recruited adult KTRs undergoing living donor KTx at the Clinic of Nephrology and Renal Transplantation, Laiko General Hospital, Athens, Greece, and their respective donors. We included pairs of individuals fulfilling the following criteria: patients assessed suitable for KTx and their respective donors assessed suitable for kidney donation, age >18 years and provision of informed written consent. Exclusion criteria were eGFR decline >30% during the last 3 months in living kidney donors, change in antihypertensive treatment during the last 6 weeks in both KTRs and donors, chronic atrial fibrillation or other arrhythmias that could interfere with proper ABPM recording and the presence of bilateral arteriovenous fistulae that could interfere with proper ABPM recording (for KTRs only). The study protocol was approved by the Institutional Review Board of Laiko General Hospital and School of Medicine, National and Kapodistrian University of Athens, Athens, Greece. All evaluations were performed according to the Declaration of Helsinki (2013 amendment).

Study protocol

All measurements were performed at the Nephrology and Renal Transplantation Center and the Cardiovascular Prevention and Research Unit of the Department of Pathophysiology, Laiko General Hospital, National and Kapodistrian University of Athens, Athens, Greece. Participants were evaluated during a scheduled morning visit at three different time points: baseline (1 month ± 10 days before scheduled KTx/donation), 3 months (±10 days) after KTx/donation and 12 months (±2 weeks) after KTx/donation.

Data for each subject were recorded on specific forms and were transferred to a purpose-built electronic data-collecting sheet. We collected information on demographics, anthropometric characteristics, comorbidities, concomitant medication and transplantation/donation-related parameters for each participant. A physical examination and venous blood sampling for routine haematological and biochemical tests were also performed at each visit. Office BP was measured at the level of the brachial artery following at least 5 min of rest using a validated oscillometric device and a cuff of appropriate size. The average of three different BP readings taken at 1-min intervals was used in the analysis.

ABPM

ABPM was performed with the Mobil-O-Graph device (IEM, Stolberg, Germany), a validated oscillometric device [24, 25] that was previously shown to provide practically identical values to a widely used ABPM monitor [26]. The device was fitted on the non-fistula arm with a cuff of appropriate size and measured BP every 15 min during the day time and every 30 min during the night time. All participants were instructed to continue their regular medication and follow their usual activities. Measurements were used for the analysis if >70% of recordings were valid with ≤2 non-consecutive day-hours with less than two valid measurements and ≤1 night-hour without valid recording for each 24-h period. To minimize the possible effect of manual BP measurements, only measurements recorded at the pre-specified time intervals at which the device was set to take measurements were used in this analysis. In the case of invalid ABPM recordings, participants were invited to undertake the ABPM again within 1 week of the original planned measurements. Pairs who failed to obtain one valid baseline ABPM recording for either the donor or the recipient were excluded from further evaluation. In addition, pairs with invalid ABPM for either the donor or the recipient at both the 3- and 12-month evaluations were also excluded from this analysis.

Definitions

Hypertension was defined as office BP ≥130/80 mmHg or use of antihypertensive medication, following the recent KDIGO guidelines [5], and ambulatory 24-h BP ≥125/75 mmHg or use of antihypertensive medication. The 24-h BP thresholds are those corresponding to the office BP thresholds, according to American College of Cardiology/American Heart Association guidelines [27]. Hypertension control was defined as the proportion of hypertensive patients achieving an office BP <130/80 mmHg or 24-h BP <125/75 mmHg.

The dipping pattern of nocturnal BP was calculated with the following formula: 1 − mean night/mean day ratio of systolic BP (SBP) (%). Patients were categorized into four groups: extreme dippers (nocturnal BP decrease of >20%), dippers (decrease of >10% but ≤20%), non-dippers (decrease of ≥0% but ≤10%) and reverse dippers (nocturnal increase in SBP) [19]. The pre-awakening morning SBP surge was calculated as the difference between the average of the 2 h after awaking minus the average of the 2 h pre-awakening, as previously described [28].

Statistical analysis

Data analysis was performed with the Statistical Package for Social Sciences version 23.0 (IBM, Armonk, NY, USA). The Shapiro–Wilk test was applied to examine the normality of distribution for quantitative variables. Continuous variables are presented as mean ± standard deviation (SD) or median [interquartile range (IQR)], depending on the normality of distribution. Categorical variables are presented as absolute frequencies and percentages [*n* (%)]. Within-group comparisons for continuous variables were performed with the paired *t*-test or Wilcoxon signed-rank test, according to the normality of the distribution. McNemar's test was used to compare paired categorical data. Finally, to evaluate the changes between the different time points before and after KTx/donation, we performed a one-way repeated-measures analysis of variance (ANOVA). Greenhouse–Geiser correction was applied to overcome the violation of the sphericity assumption. *P*-values <.05 (two-tailed) were considered statistically significant for all comparisons.

RESULTS

Baseline characteristics of the study participants

A total of 52 KTRs and their respective donors fulfilled the aforementioned inclusion and exclusion criteria and consented to participate. Of these, five KTRs and seven donors failed to have a valid 24-h ABPM at baseline; one KTR had acute graft rejection. Consequently, nine kidney transplant donor–recipient pairs were excluded from further evaluation. During follow-up, two KTRs and their respective donors were lost, while one kidney donor had an invalid ABPM recording at both the 3- and

Table 1. Baseline demographic, anthropometric and clinical characteristics of study participants

Variable	KTRs ($n = 40$)	Donors ($n = 40$)
Female gender, *n* (%)	12 (30.0)	29 (72.5)
Age (years)	45.61 ± 13.93	56.48 ± 12.21
Dialysis vintage previous to transplantation (months), median (IQR)	37.00 (22.4–54.88)	
Dialysis modality prior to KTx (HD/PD/pre-emptive), *n* (%)	27 (67.5%)/4 (10.0%)/9 (22.5%)	
BMI (kg/m^2)	26.88 ± 4.98	25.07 ± 5.46
Hypertension, *n* (%)	39 (97.5)	11 (27.5)
Diabetes, *n* (%)	5 (12.5)	1 (2.5)
Dyslipidaemia, *n* (%)	15 (37.5)	7 (17.5)
CVD, *n* (%)	2 (5.0)	3 (7.5)
CAD, *n* (%)	2 (5.0)	1 (2.5)
Stroke, *n* (%)	0 (0.0)	2 (5.0)
PAD, *n* (%)	0 (0.0)	0 (0.0)
Smoking, *n* (%)	8 (20.0)	10 (25.0)
Office SBP (mmHg)	133.8 ± 20.3	122.9 ± 14.9
Office DBP (mmHg)	85.2 ± 15.6	75.6 ± 9.5
Number of antihypertensive drugs	1.65 ± 1.03	0.38 ± 0.77
ACEi/ARB, *n* (%)	8 (20.0)	6 (15.0)
CCBs, *n* (%)	22 (55.0)	4 (10.0)
MRAs, *n* (%)	0 (0.0)	0 (0.0)
β-blockers, *n* (%)	21 (52.5)	3 (7.5)
α-blockers, *n* (%)	1 (2.5)	0 (0.0)
Nitrates, *n* (%)	1 (2.5)	0 (0.0)
Central acting agents, *n* (%)	3 (7.5)	0 (0.0)
Diuretics, *n* (%)	8 (20.0)	2 (5.1)
Statins, *n* (%)	12 (30.0)	7 (17.5)
WBC (×10^3/μL)	7.42 ± 2.69	6.38 ± 1.52
Haemoglobin (g/dL)	11.42 ± 1.28	13.46 ± 1.57
eGFR (CKD-EPI; mL/min/1.73 m^2)	7.52 ± 2.39	93.95 ± 13.44
Creatinine (mg/dL)	7.99 ± 0.74	0.74 ± 0.13
Urea (mg/dL)	130.68 ± 41.56	31.48 ± 7.60
Uric acid (mg/dL)	5.76 ± 1.98	4.61 ± 1.10
Sodium (mEq/L)	138.83 ± 2.11	141.55 ± 2.01
Potassium (mEq/L)	4.94 ± 0.55	4.56 ± 0.33
Calcium (mg/dL)	9.36 ± 0.87	9.61 ± 0.27
Phosphorus (mg/dL)	4.94 ± 1.37	3.40 ± 0.53
PTH (pg/mL), median (IQR)	177.00 (119.00–381.00)	41.6 (30.88–58.00)
CRP (mg/L), median (IQR)	2.00 (0.95–3.64)	1.18 (0.56–2.29)
Total cholesterol (mg/dL)	156.58 ± 42.93	192.87 ± 38.00
Triglycerides (mg/dL)	208.45 ± 125.3	117.32 ± 64.97
Ferritin (ng/mL), median (IQR)	301.00 (174.3–712.00)	81.6 (47.00–136.00)

Values are presented as mean ± SD unless stated otherwise. HD, haemodialysis; PD, peritoneal dialysis; BMI, body mass index; PAD, peripheral artery disease; CAD, coronary artery disease; WBC, white blood cell; PTH, parathormone; CRP, C-reactive protein; KTx, kidney transplantation; CVD, cardiovascular disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACEi, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CCB, calcium channel blockers; MRAs, mineralocorticoid receptor antagonists. CVD, cardiovascular disease; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; MRA, mineralocorticoid receptor antagonists.

12-month evaluations. Thus a total of 40 KTRs and their respective donors represented the final study population of this analysis. Following the study protocol, all 40 pairs had full ABPM sets at baseline evaluation, while 36 pairs also had full ABPM sets at the 3-month evaluation and 32 full ABPM sets at the 12-month evaluation. All KTRs in this study followed the common immunosuppression protocol of our centre, which includes quick tapering of steroids and lower calcineurin inhibitor blood levels and mycophenolate mofetil doses a few months after transplantation, without the withdrawal of any of these regimens.

Table 1 presents baseline demographics and clinical and laboratory characteristics for the two study groups. A total of 40 KTRs (12 females) with a mean age of 45.61 ± 13.93 years and 40 living kidney donors (29 females, mean age 53.91 ± 17.25 years) were included in the analysis. With regard to major comorbidities, hypertension was the most common among them, both in KTRs (97.5%) as well as in kidney donors (27.5%). At baseline, mean office SBP/diastolic BP (DBP) was 133.75 ± 20.33/85.15 ± 15.62 mmHg in KTRs and 122.85 ± 14.90/75.63 ± 9.51 mmHg in kidney donors.

Office BP levels in KTRs were progressively reduced during follow-up [SBP: 133.8 ± 20.3 versus 126.0 ± 11.8 versus 122.8 ± 12.7 mmHg (ANOVA $P = .064$) and DBP: 85.2 ± 15.6 versus 77.6 ± 9.2 versus 76.1 ± 9.9 mmHg ($P = .008$)]. The mean number of antihypertensive drugs required was reduced from baseline to 3 months (1.65 ± 1.03 versus 1.27 ± 1.01; $P = .042$) and remained stable thereafter (1.25 ± 1.08; ANOVA $P = .108$). In contrast, no changes were noted in office BP [122.9 ± 14.9 versus 120.4 ± 14.2 versus 122.6 ± 14.7 mmHg ($P = .607$)] and DBP [75.6 ± 9.5 versus 74.9 ± 9.9 versus 73.9 ± 10.0 mmHg ($P = .927$)] or number of antihypertensive drugs (0.38 ± 0.77 versus 0.25 ± 0.67 versus 0.22 ± 0.61; $P = .146$) in kidney donors. Changes in clinical and laboratory parameters between the

Table 2. Ambulatory BP levels at baseline and 3 and 12 months after kidney transplant surgery in KTRs

Variable	Baseline, mean ± SD	3 months, mean ± SD	P-value	12 months, mean ± SD	P-value
24-h period					
SBP (mmHg)	131.9 ± 13.3	126.4 ± 11.9	.075	123.9 ± 10.3	.009
DBP (mmHg)	86.7 ± 11.5	82.2 ± 8.1	.043	80.3 ± 8.5	.009
MBP (mmHg)	107.4 ± 11.9	102.4 ± 9.2	.053	100.2 ± 8.8	.007
PP (mmHg)	45.2 ± 7.0	44.3 ± 8.1	.412	43.6 ± 6.0	.190
HR (mmHg)	76.0 ± 9.7	74.9 ± 10.8	.419	70.4 ± 8.7	<.001
Day time					
SBP (mmHg)	132.6 ± 13.8	126.6 ± 11.5	.068	124.6 ± 10.2	.009
DBP (mmHg)	87.6 ± 11.8	82.7 ± 8.3	.038	81.2 ± 8.1	.011
MBP (mmHg)	108.2 ± 12.2	102.8 ± 9.1	.046	101.0 ± 8.6	.008
PP (mmHg)	45.1 ± 7.2	43.9 ± 7.9	.421	43.4 ± 6.2	.174
HR (mmHg)	77.2 ± 10.0	76.3 ± 11.2	.533	72.4 ± 9.3	.002
Night time					
SBP (mmHg)	130.0 ± 14.7	124.9 ± 13.7	.117	121.8 ± 13.5	.021
DBP (mmHg)	83.8 ± 12.6	80.2 ± 8.7	.157	77.5 ± 10.7	.019
MBP (mmHg)	105.0 ± 12.9	100.7 ± 10.1	.125	97.8 ± 11.5	.017
PP (mmHg)	46.2 ± 8.7	44.8 ± 9.7	.250	44.3 ± 7.2	.254
HR (mmHg)	72.0 ± 10.0	69.5 ± 11.3	.126	64.5 ± 8.1	<.001

SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean arterial blood pressure; PP, pulse pressure; HR, heart rate.
A P-value of <.05 (two-tailed) was considered statistically significant for all comparisons.

baseline and 12-month evaluation in KTRs and living kidney donors are presented in Supplementary data, Table S1.

Ambulatory BP levels and trajectories in KTRs

The mean ambulatory BP levels at baseline and 3 and 12 months after kidney transplant surgery for KTRs are depicted in Table 2. At the 3-month evaluation, the total 24-h SBP levels were marginally lower (131.9 ± 13.3 versus 126.4 ± 11.9 mmHg; $P = .075$) and the 24-h DBP levels were significantly lower (86.7 ± 11.5 versus 82.2 ± 8.1 mmHg; $P = .043$) compared with baseline. Following numerical reductions in both SBP and DBP levels, no significant differences between the baseline and 3-month evaluation were observed for 24-h pulse pressure (PP; 45.2 ± 7.0 versus 44.3 ± 8.1 mmHg; $P = .412$, respectively).

In the 12-month evaluation, 24-h SBP (131.9 ± 13.3 versus 123.9 ± 10.3 mmHg; $P = .009$) and DBP (86.7 ± 11.5 versus 80.3 ± 8.5 mmHg; $P = .009$) were both significantly decreased compared with baseline, as shown in Table 2. This was also the case for 24-h mean BP (MBP) levels (107.4 ± 11.9 versus 100.2 ± 8.8 mmHg; $P = .007$). In addition to the above, both day time SBP/DBP (132.6 ± 13.8/87.6 ± 11.8 versus 124.6 ± 10.2/81.2 ± 8.1 mmHg; $P = .009/.011$) and night time SBP/DBP (130.0 ± 14.7/83.8 ± 12.6 versus 121.8 ± 13.5/77.5 ± 10.7 mmHg; $P = .021/.019$) were significantly lower 12 months after kidney transplant surgery compared with baseline.

Figure 1 presents the results of one-way repeated measures ANOVA of the mean 24-h SBP and DBP levels at the baseline, 3- and 12-month evaluations. As shown in the figure, both SBP and DBP presented a significant gradual decrease over time {SBP [$F(1.463, 39.505) = 3.616$; $P = .049$, partial $\eta^2 = 0.118$]; DBP [$F(1.374, 37.089) = 11.34$; $P = .055$, partial $\eta^2 = 0.116$]}. Figure 2 depicts the trajectories of the hourly mean SBP and DBP levels during a 24-h recording evaluated at the three different study time points. In agreement with the mean ambulatory BP level comparisons, a progressive decrease in the SBP and DBP curves between baseline and the 3- or 12-month evaluations is noted.

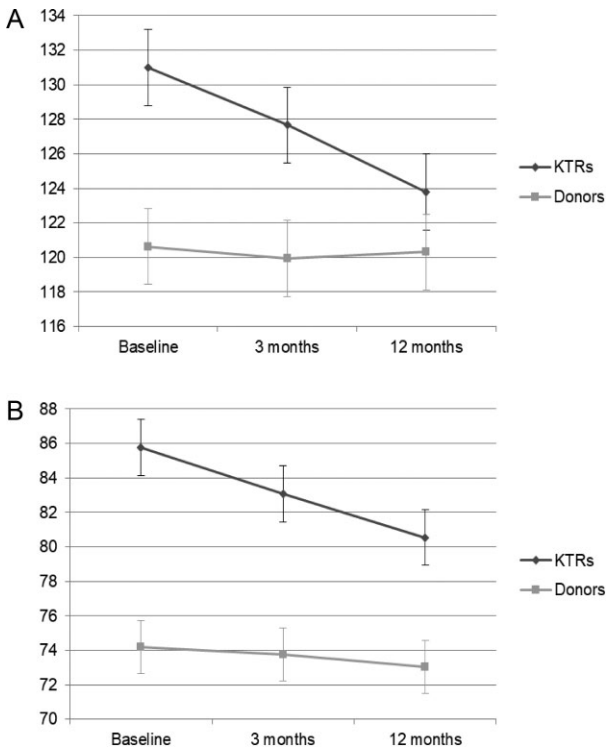


FIGURE 1: Estimated marginal means of (**A**) 24-h SBP and (**B**) 24-h DBP in KTRs and living kidney donors at baseline and 3 and 12 months after kidney transplant surgery.

Ambulatory BP levels and trajectories in living kidney donors

The mean ambulatory BP levels of kidney donors at baseline and 3 and 12 months after kidney transplant surgery are presented in Table 3. At the 3-month evaluation, the 24-h SBP (118.5 ± 11.6 versus 118.2 ± 12.8 mmHg; $P = .626$), DBP (73.2 ± 8.1 versus

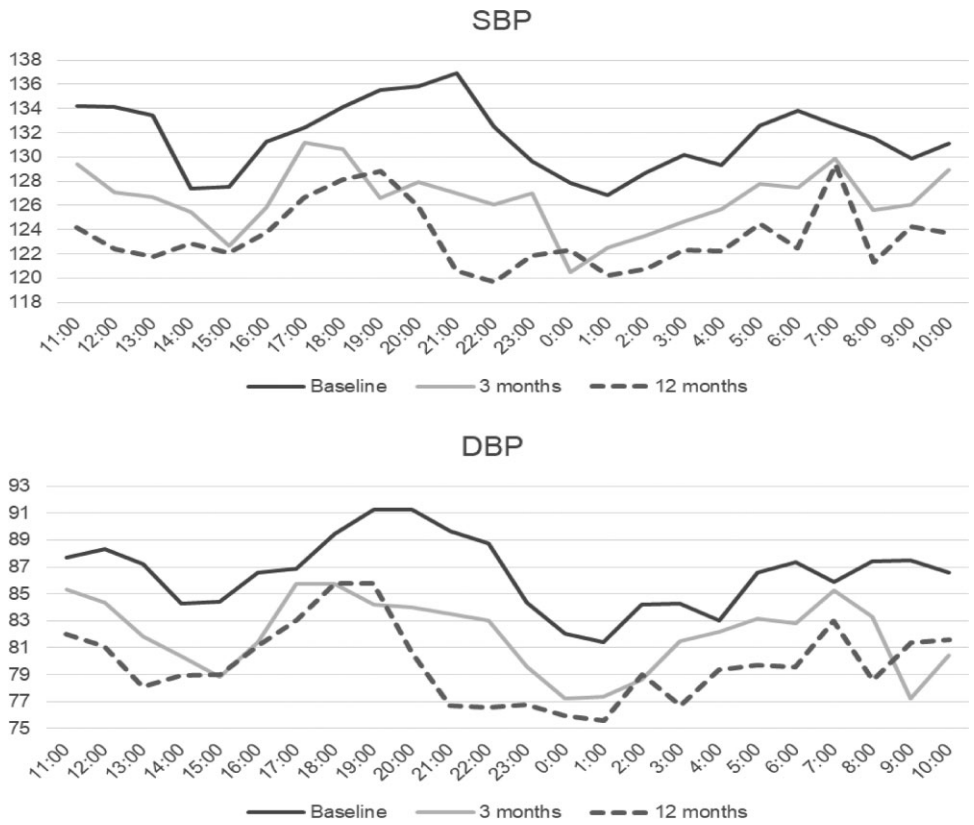


FIGURE 2: Trajectories of peripheral SBP and DBP in KTRs during the 24-h recording period.

Table 3. Ambulatory BP levels at baseline and 3 and 12 months after kidney transplant surgery in living kidney donors

Variable	Baseline, mean ± SD	3 months, mean ± SD	*P*-value	12 months, mean ± SD	*P*-value
24-h period					
SBP (mmHg)	118.5 ± 11.6	118.2 ± 12.8	.626	119.2 ± 11.4	.748
DBP (mmHg)	73.2 ± 8.1	72.8 ± 8.4	.773	73.2 ± 8.2	.360
MBP (mmHg)	94.0 ± 8.8	93.6 ± 9.8	.678	94.2 ± 9.0	.554
PP (mmHg)	45.2 ± 8.7	45.4 ± 8.0	.577	46.0 ± 7.9	.535
HR (mmHg)	69.1 ± 8.4	68.5 ± 6.7	.816	70.4 ± 9.1	.691
Day-time					
SBP (mmHg)	121.1 ± 12.1	121.0 ± 13.6	.688	121.3 ± 11.0	.552
DBP (mmHg)	75.4 ± 8.8	75.0 ± 8.5	.789	75.4 ± 7.9	.352
MBP (mmHg)	96.3 ± 9.4	96.1 ± 10.3	.727	96.4 ± 8.5	.450
PP (mmHg)	45.6 ± 9.2	46.0 ± 8.7	.700	45.9 ± 8.2	.905
HR (mmHg)	71.9 ± 9.1	70.8 ± 7.1	.846	72.8 ± 9.3	.905
Night-time					
SBP (mmHg)	111.2 ± 12.1	110.6 ± 12.3	.601	113.1 ± 13.8	.836
DBP (mmHg)	67.0 ± 8.0	66.6 ± 8.8	.803	66.5 ± 9.6	.450
MBP (mmHg)	87.3 ± 9.2	86.7 ± 9.8	.660	87.8 ± 11.0	.802
PP (mmHg)	44.2 ± 8.1	43.9 ± 7.7	.474	46.5 ± 8.0	.107
HR (mmHg)	60.9 ± 7.9	61.9 ± 6.8	.143	63.5 ± 9.7	.049

SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean arterial blood pressure; PP, pulse pressure; HR, heart rate.

72.8 ± 8.4; $P = .773$), MBP and PP levels did not practically change compared with baseline. Similarly, no significant changes in day time SBP/DBP and night time SBP/DBP were observed.

At the 12-month evaluation, no significant changes in 24-h SBP (118.5 ± 11.6 versus 119.2 ± 11.4 mmHg; $P = .748$), DBP (73.2 ± 8.1 versus 73.2 ± 8.2; $P = .360$), MBP and PP levels compared with the baseline evaluation were noted. Similar observations were made for SBP and DBP levels during the respective day time (SBP/DBP: 121.1 ± 12.1/75.4 ± 8.8 versus 121.3 ± 11.0/75.4 ± 7.9 mmHg; $P = .552/.352$) and

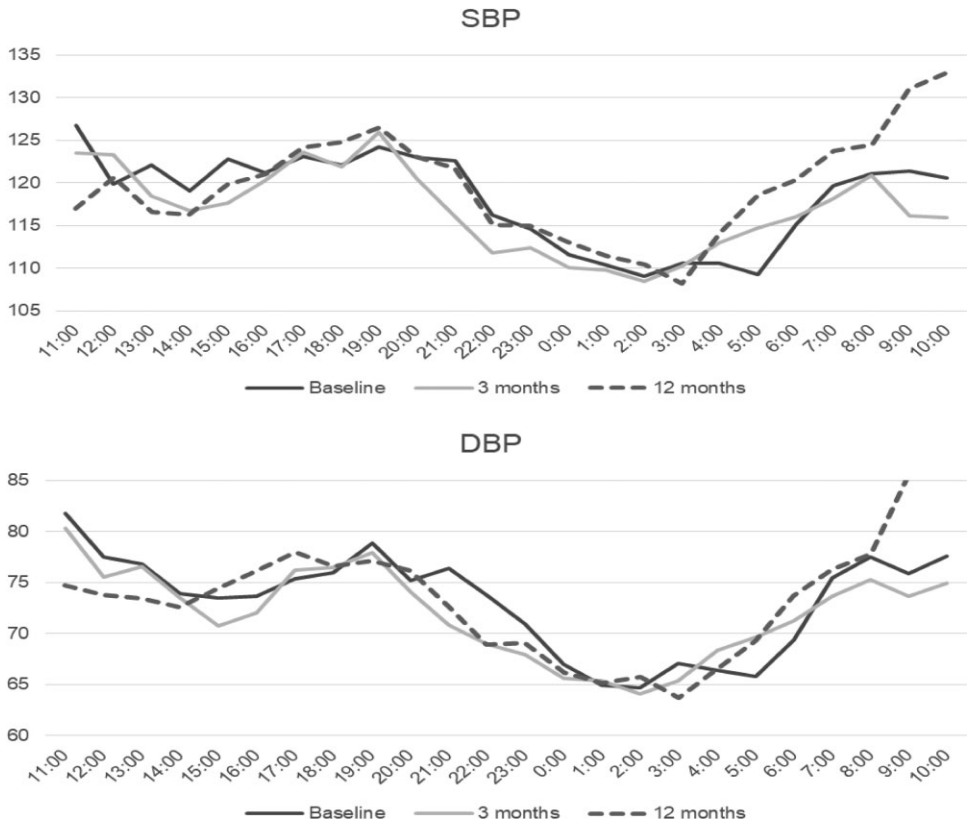


FIGURE 3: Trajectories of peripheral SBP and DBP in living kidney donors during the 24-h recording period.

night time periods (SBP/DBP: 111.2 ± 12.1/67.0 ± 8.0 versus 113.1 ± 13.8/66.5 ± 9.6 mmHg; $P = .836/.450$).

The results of one-way repeated measures ANOVA of the mean 24-h SBP and DBP levels of kidney donors at baseline and the 3- and 12-month evaluations for kidney donors are depicted in Fig. 1. No differences in the mean SBP/DBP levels over time were observed {SBP [$F(2, 52) = 0.067$; $P = .936$, partial $\eta^2 = 0.003$]; DBP [$F(2, 52) = 0.467$; $P = .630$, partial $\eta^2 = 0.018$]}. Furthermore, the trajectories of the hourly mean SBP levels of kidney donors during a 24-h recording evaluated at baseline and 3 and 12 months are practically overlapping. A similar pattern was observed for the trajectories of 24-h DBP at the three different study time points (Fig. 3).

BP phenotypes, dipping patterns and pre-awakening surge of SBP in KTRs and living kidney donors

Figure 4A and B depicts the different BP phenotypes of KTRs and donors at baseline and the 3- and 12-month evaluations. As shown in the figure, the distribution of BP phenotypes showed a beneficial change in KTRs between baseline and the 12-month evaluation (baseline concordant lack of BP control by both office and ABPM, concordant control, white-coat hypertension and masked hypertension were apparent in 67.5%, 7.5%, 5.0% and 20.0% versus 50.0%, 25.0%, 0.0% and 25.0%; $P = .146$). The relevant percentages in donors were 35.0%, 32.5%, 20.0% and 12.5% versus 37.5%, 40.6%, 12.5% and 9.4% ($P = .677$).

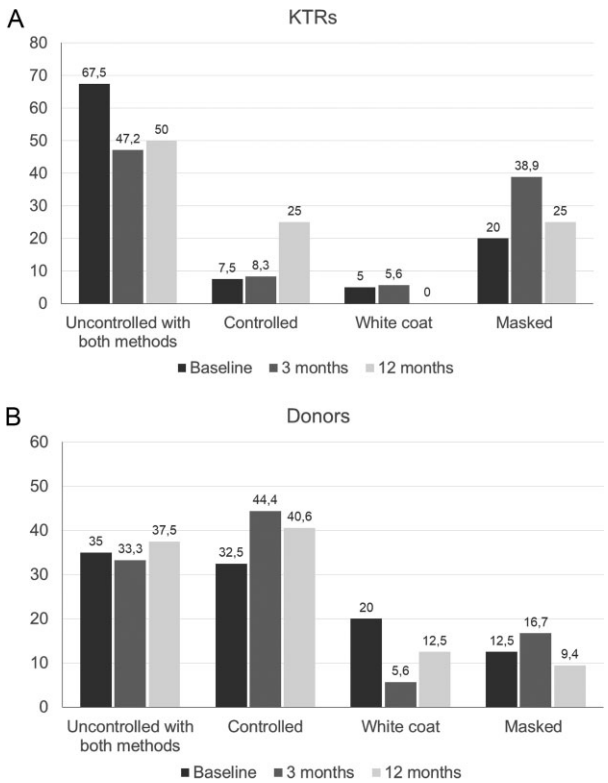


FIGURE 4: BP phenotypes of (**A**) kidney transplant recipients (KTRs) and (**B**) living kidney donors at baseline, 3 and 12 months after kidney transplant surgery.

Supplementary data, Table S2 presents the dipping patterns of KTRs and donors at baseline and the 3- and 12-month evaluations according to four-type (reverse dipper, non-dipper, dipper, extreme dipper) categorization. No significant changes were observed in the dipping patterns of either group between baseline and 3 and 12 months, respectively. The average pre-awakening SBP surge at baseline and the 12-month evaluation was 2.63 ± 15.97 versus 9.47 ± 15.06 in KTRs ($P = .144$) and 9.91 ± 10.85 versus 7.15 ± 10.78 in donors ($P = .373$).

DISCUSSION

The present study showed that KTRs experienced a significant gradual decrease in ambulatory SBP and DBP at both the 3- and 12-month evaluations following KTx. Day time and night time SBP and DBP followed a similar pattern, corresponding with a progressive decrease in the 24-h SBP and DBP trajectories at the 3- and 12-month evaluations. In contrast, no differences in the mean 24-h, day time, or night time BP levels or in the 24-h BP trajectories between the baseline and the 3- and 12-month evaluations were observed in the living kidney donors. Similar changes were observed in office BP for KTRs and donors, respectively. A reduction in the number of antihypertensive agents was observed in KTRs but not in donors. No significant differences were noted in dipping patterns in either of the groups between the baseline and 3- and 12-month evaluations.

Hypertension is the predominant risk factor for CVD and has been associated with impaired graft and patient survival in KTRs [10]; its prevalence is particularly high (70–95%) [9, 29], but its control rates are rather unsatisfactory at 40–60% [9]. Traditionally, hypertension diagnosis and management in KTRs was based on office BP measurements. However, office BP has several limitations in the diagnosis and management of hypertension compared with the gold standard of BP measurement, which is 24-h ABPM [12, 13]. The latter enables identification of white coat and masked hypertension phenotypes, which are particularly common in KTRs [30], and displays stronger associations than office BP with target-organ damage [11]. In view of the above, recent guidelines and consensus documents highlight the need of more extended ABPM use in the diagnosis and management of hypertension in KTRs [5, 14].

Previous studies indicated the positive impact of KTx on ambulatory BP. In 123 children and young adults receiving a kidney transplant, Hamdani *et al.* [18] showed that the prevalence of elevated ambulatory BP levels decreases 12 months after surgery, due to the increased number of KTRs with controlled hypertension. Moreover, in a prospective study including 48 adult KTRs, a significant decrease in the proportion of hypertensive patients with sustained elevated BP and in the number of anti hypertensive medications used was noted 12 months after KTx, whereas the MBP levels did not differ from baseline (125.0 ± 10.2 versus 121.4 ± 10.9; $P = .10$) [31]. Finally, in a recent study evaluating changes in ambulatory BP in pairs of KTRs and their counterpart kidney donors with ABPM 12 months after KTx, there was an improvement of ∼8/4 mmHg in 24-h SBP/DBP levels in the transplant recipients at 12 months, despite the lower number of antihypertensive medications used [17]. It has to be noted, however, that the abovementioned studies have examined the average 24-h BP levels at one time point post-transplantation and not a detailed ambulatory BP profile with consecutive evaluations. Several pathogenetic mechanisms have been proposed to play a significant role in BP lowering, including improvement of sodium and volume overload and clearance of uraemic toxins related to kidney function improvement [17]. Other plausible mechanisms may be decreased arterial stiffness [32], change from a sodium-sensitive to a sodium-resistant hypertension phenotype, lowering of the activity of the renin–angiotensin system and sympathetic system and improvement in endothelial function observed after KTx [33, 34].

Our study expands the existing knowledge by showing that KTRs experienced a significant gradual decrease in 24-h SBP/DBP levels at both the 3- and 12-month evaluations following KTx. In addition, it evaluated separately day- and night time SBP and DBP and hourly 24-h SBP and DBP trajectories, all of which followed a similar pattern at the 3- and 12-month evaluations. Of note, these significant reductions were followed by a reduction in the average number of antihypertensive medications used, indicating an overall beneficial effect of KTx on the ambulatory BP profile. In addition, we observed an overall beneficial effect of KTx on BP control; the proportion of KTRs with concordant lack of control by both office and ABPM was reduced, whereas the percentage of patients with concordant control of BP was almost quadrupled. Despite these beneficial effects, the rates of uncontrolled hypertension in our cohort are considered high and are similar to those reported in recent meta-analyses [30]. In addition, no significant changes were noted in dipping patterns, with the proportion of non-dippers and reverse dippers remaining considerably high (53.1% and 31.3%, respectively), similar to previously reported rates (42% and 34%) 12 months after KTx [33]. A beneficial effect in the blunted baseline pre-awakening surge was observed, probably in line with a modest decrease in reverse dipper pattern.

Moreover, studies using 24-h ABPM have shown that kidney donation does not seem to affect the BP levels of donors at short-, mid- and long-term follow-up after nephrectomy [20–23, 35]. In a previous study including 58 living kidney donors [36], 24-h BP levels and dipping profiles remained unchanged from pre-donation to 6 months post-donation. In the aforementioned study from Buus *et al.* [17] and another study in 168 kidney donors [37], ambulatory BP levels also remained unchanged at 1 year after kidney donation. Other studies showed no differences in ambulatory BP levels up to 10 years after donation [20, 38]. Again, however, the majority of these studies offered information on mean 24-h BP levels at a single post-transplant time point. The present study expands these observations by offering a detailed evaluation of the BP profile in living kidney donors and showing practically no differences in the mean 24-h, day time, or night time BP level or in the 24-h BP trajectories between baseline and the 3- and 12-month evaluations. Moreover, we found a slight increase in the proportion of kidney donors with concordant BP control by both office and 24-h BP, as well as a slight decrease in white coat hypertension. Kidney donation did not seem to significantly affect the prevalence of masked and sustained uncontrolled hypertension or the dipping BP profile.

Our study has strengths and limitations. It is the first to investigate in parallel the full ambulatory BP profile and trajectories in pairs of KTRs and their counterpart kidney donors. By studying donor–recipient pairs, our work expands the aforementioned data for KTRs and donors by adding detailed information on the effects of the specific kidney that is transplanted between each pair on changes in BP parameters (positive for KTRs and neutral for donors). This study followed a prospective design and applied a strict methodology using valid 24-h ABPM readings at three different study time points. One limitation is the 12-month duration of the follow-up period, which does not enable us to investigate possible long-term effects of kidney transplantation/donation. Another potential limitation is

that this is a single-centre study in mainly Caucasian KTRs and kidney donors, thus the conclusions should be applied with caution to other populations.

In conclusion, the present study is the first to evaluate in parallel ambulatory BP levels and trajectories in KTRs and their respective living kidney donors in the short- and mid-term following KTx. KTRs experienced a gradual decrease in ambulatory SBP and DBP levels corresponding to a progressive decrease in the 24-h SBP and DBP trajectories at both the 3- and 12-month evaluations following KTx. In contrast, no differences in the mean ambulatory BP levels or in the 24-h BP trajectories at the same intervals were observed for the living kidney donors. These results add conclusively to the evidence that KTx significantly improves the ambulatory BP profile of the KTRs without even mildly affecting the ambulatory BP profile of kidney donors in the short- and mid-term. Future studies investigating the potential long-term effects of kidney transplantation/donation on the abovementioned ambulatory BP parameters would be of interest.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

FUNDING

This article was not supported by any source and represents an original effort of the authors.

CONFLICT OF INTEREST STATEMENT

The authors state that they do not have any conflicts of interest to disclose regarding this article.

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