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Short Term Reproducibility of Ambulatory Blood Pressure Monitoring in Autosomal Dominant Polycystic Kidney Disease

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Abstract

Background and objectives—Non-dipping defined as a less than 10% decline in night/day ration of blood pressure using 24 hour ambulatory blood pressure monitoring (ABPM) is associated with poor cardiovascular outcomes. However, its reproducibility has been questioned in autosomal dominant polycystic kidney disease (ADPKD).

Design, setting, participants and measurements—25 of 29 recruited hypertensive or prehypertensive ADPKD patients completed ABPM on two occasions, 7–15 days apart, on a stable antihypertensive regimen. Day and night time were defined as 6:00–21:59 and 22:00–5:59. Correlation (Corr) and concordance (Conc) coefficients for systolic (SBP), diastolic blood pressure (DBP) and heart rate were determined based on night/day (N:D) and asleep/awake (A:A) periods. Consistency of dipping was assessed by using Cohen's Kappa statistics.

Results—Mean (±SD) for age, estimated GFR, differences in D-N night SBP and DBP were 43.12 (8.55) years, 63.1 (20.5) mL/min, 11.74(8.2) mmHg and 10.82 (6.4) mmHg respectively. 17/25 subjects (68%) and 18/25 (72%) maintained the same dipping category based on D:N or A:A separation. Cohen's Kappa was 0.34 for D:N and 0.38 for A:A ratios. Correlation and concordance coefficients were 0.89 and 0.88 for daytime SBP, 0.91 and 0.91 for daytime DBP, 0.79 and 0.78 for nighttime SBP, 0.81 and 0.80 for nighttime DBP, 0.58 and 0.56 for N:D ratio of SBP, 0.56 and 0.53 for N:D ratio of DBP. Coefficients for A:A ratios were almost identical to N:D values except for A:A ratios of SBP (0.69 and 0.67) and DBP (0.48 and 0.45).

Conclusions—Repeated measures of SBP and DBP, 7–15 days apart, are highly correlative and concordant in the studied population but non-dipping, even though predominant, was found to be modestly reproducible.

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited renal disease affecting 1/1000 live births. ADPKD is due to mutations in the PKD1 and PKD2 genes and progresses to end stage renal disease (ESRD) at a mean age of 55 and 69 years respectively [1]. Hypertension onset is early with a mean age of 31 years and a prevalence of 22% in pediatric population. Hypertension is strongly associated with hyperactivity of the renin-angiotensin-aldosterone system (RAAS), presenting in 60% of patients prior to onset of renal insufficiency, and representing a major risk factor for progression to renal failure and cardiovascular mortality [2–4]. Importantly, hypertension is also the most preventable and treatable associated condition with ADPKD [5] and the control of hypertension obviously depends on using the most accurate and tolerable method of blood pressure monitoring.

The most common non-invasive methods of blood pressure monitoring include office (also called clinic) blood pressure monitoring (OBPM) using oscillometric or aneroid devices, self-measured home blood pressure monitoring (HBPM) using oscillometric devices, and 24-hour ambulatory blood pressure monitoring (ABPM) using a computerized oscillometric device. OBPM represents the most commonly used method in clinical practice. Current guidelines for diagnosis and management of hypertension outlined in the 7th report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC-7) are based on OBPM with some reference to ABPM but with little focus on self-measured HBPM [6]. However, white-coat hypertension (office blood pressures readings higher than home readings) and masked hypertension (the opposite) which are present in up to 30% of subjects limit the use of OBPM. [7]. Therefore, out-of-office blood pressure monitoring by ABPM or HBPM should play a significant role in the care of hypertension and are often necessary. Importantly, HBPM and ABPM are more reproducible and reliable than OBPM [8] and OBPM readings have been reported to be 7–17 mmHg higher for SBP and 5–14 mm Hg higher for DBP compared to ABPM and HBPM. Whether circadian differences in blood pressure differ between out of office blood pressure measures is unclear, however the difference between daytime ABPM readings and HBPM are insignificant [9].

HBPM and ABPM predict end-organ damage (left ventricular hypertrophy or LVH, arterial stiffness index and albuminuria) in essential hypertension and chronic kidney disease more reliably than OBPM [10–11]. However, only ABPM provides an insight to the nocturnal and early morning variations of blood pressure. The lack of nocturnal drop in blood pressure or non-dipping, has been associated with end organ damage including LVH, congestive heart failure, stroke, acute coronary events, microalbuminuria, decline in glomerular filtration rate (GFR), progression to end stage renal disease (ESRD) and all cause mortality in both essential hypertension and in ADPKD [12–21].

Despite these compelling data regarding home and ambulatory blood pressure predicting patient outcomes, Palatini et al reported poor reproducibility of the nocturnal dipping status in hypertensive patient populations [22]. In a subsequent review of 12 studies, Parati et al showed a wide range of reproducibility rates of nocturnal dipping categorization (29.5% – 92%) in normotensive, treated and untreated hypertensive, type-I and type-II diabetic, and chronic kidney disease patients [23]. In ADPKD there is only one study comparing 3 sets of ABPM readings over 12 months, at least 3 months apart, in 30 hypertensive ADPKD patients. This study showed a consistent of dipping status in 43% of cases between two sets and 36.6% between the three sets of ABPM [24]. However there were differences in therapeutic regimens (especially regarding the use of blockers of the RAAS) and significant changes in renal function due to the length of the study. Therefore, the utility of what

appears to be the main advantage of ABPM over HBPM remains uncertain in ADPKD population. Our study aimed to establish the short term reproducibility of ABPM in treated hypertensive ADPKD patients.

Methods

Recruitment

We used the general infrastructure of the ongoing HALT-PKD trials for recruitment of the subjects. Design and implementation of HALT-PKD trials have extensively been detailed elsewhere [25]. Briefly, HALT-PKD is a combination of two concurrent randomized double blinded and placebo-controlled trials evaluating the effect of multilevel blockade of the renin-angiotensin-aldosterone system in hypertensive or prehypertensive ADPKD patients, by using angiotensin converting enzyme inhibitor (ACE-I) alone vs. ACE-I + an angiotensin receptor blocker (ARB). HBPM was the method of choice to guide therapeutic decisions regarding dose titration and addition of new antihypertensive agents. Figure-1 shows the place of ambulatory blood pressure monitoring within the general frame of HALT-PKD trials.

Our recruitment goal was 25 hypertensive patients at Emory University and the Mayo clinic, MN. Inclusion criteria were identical to the HALT-PKD participation criteria with additional inclusion exclusion criteria including: providing informed consent, absence of allergic reaction to rubber (blood pressure cuff), absence of acute illnesses and absence of limited mobility (wheelchair bound or bedridden), absence of night shift working, and completion of the titration phase of the HALT-PKD trial and on a stable antihypertensive regimen. This study protocol was approved by the HALT-PKD steering committee and the Institutional Review Boards (IRB) of Emory University and Mayo Foundation. All potential subjects underwent informed consent prior to study initiation.

Ambulatory blood pressure monitoring procedures

Spacelab-90207 monitors (Spacelabs-Redmond, WA) were used for ABPM approved by the British Society of Hypertension (BSH) and the American Association for Medical Instrumentations (AAMI). The two sets of ABPM were obtained under similar conditions 7–15 days apart. The appropriate cuff size was used on the non-dominant arm. Patients were instructed to avoid removing the monitor, showering, bathing and engaging in vigorous exercise. Blood pressure readings were measured every 20 minutes during the day (06:00 to 21:59) and every 30 minutes during the night (22:00 to 05:59). In case of first unsuccessful attempt, the monitor made 3 additional attempts to record a BP reading. For each subject, ABPMs were performed both on a similar working or non-working day. Physical activity, stress and the time of falling asleep and waking up were recorded in a diary. We did not eliminate the transition hour data points. ABPM was considered adequate if it contained more than 50 blood pressure readings, with at least one measurement every hour and less than 10% erroneous or repeated readings.

Data from ABPM were retrieved and transcribed into Excel format. Demographic and medical data were retrieved from the main HALT-PKD trial database. The HALT-PKD Data Coordinating Center monitored the integrity of study procedures on an annual basis.

Data analysis and statistical methods

The average daytime and nighttime systolic and diastolic pressures were defined as the mean of readings over the day and night periods. Mean arterial pressure was defined as $DBP + [(SBP-DBP) / 3]$. Heart rate was defined as the number of heart beats per minute during blood pressure measurements. Pulse pressure was defined as the difference between SBP

and DBP. Nocturnal dipping was defined as a night:day ratio of SBP and DBP < 0.9 and non-dipping as a ratio ≥ 0.90

A sample size of 25 was determined to be adequate to have 80% power to detect any correlation larger than 0.4 between SBP, DBP, and dipping status comparing the two sets of ABPM, at a significance level alpha 0.05.

Correlation and concordance coefficient between Day-1 and Day-2 were calculated for the following parameters: SBP, DBP, MAP, heart rate, Pulse Pressure and the N:D or A:A ratios of SBP and DBP difference between Day-1 and Day-2. Concordance coefficient (ρ_c) is defined as:

$$\rho_c = \frac{2\rho\sigma_x\sigma_y}{\sigma_x^2 + \sigma_y^2 + (\mu_x - \mu_y)^2},$$

where μ_x and μ_y are the means for the two variables and σ_x^2 and σ_y^2 are the corresponding variances. ρ is the correlation coefficient between the two variables. Concordance coefficients are more appropriate for reproducibility studies since they represent the spread of the data points around to the line of identity whereas correlation coefficients compare them to a regression line [26].

The reproducibility of dipping status was determined by estimating the proportion of patients who remained in the same dipping category. Cohen's Kappa statistics were used to compare those proportions [27]. We also considered the N:D and A:A ratios of SBP and DBP as continuous variables and calculated Pearson correlation coefficients and concordance coefficients for each measure comparing Day-1 and Day-2. Univariate analysis using either Fisher's exact test or Wilcoxon test were performed to look for potential associations between consistency of dipping and predictor variables. Finally we performed univariate analysis between then;D and A:A ratios of SBP (and DBP) and different predictor variables. Due to the number of participants (n=25), logistic or linear regression were not deemed to be applicable. All data analysis was performed using SAS 9.2 (SAS Institutes Cary, NC)

Results

29 subjects (22 at Emory University and 7 at Mayo clinic) were consented. One subject could not tolerate the blood pressure cuff, two subjects only completed one set of ABPM and one had an inadequate number of readings. 25 subjects successfully completed two sets of ABPM. Characteristics of the four subjects who were not included in the analysis did not differ from the study cohort (data not shown).

The cohort was composed of middle aged (mean age 43.1 years), non-smoking (96%), Caucasian subjects (92%) with a slight predominance of females (52%) (Table 1). Renal function was fairly well preserved (mean serum creatinine was 1.29 mg/dl and mean eGFR 63 ml/min/1.73 m²). Duration of hypertension was 9.6 years and blood pressure was extremely well controlled at the time of enrollment into this study (mean SBP and DBP 113.6 and 71.7 mmHg respectively).

Blood pressure readings were similar between day-1 and day-2 both by fixed clock and asleep-awake separation of day and night (Table-2). The average daytime SBP were 121.9 vs. 120.4 mmHg and average DBPs 77.6 and 77.1 mmHg ($p < 0.05$ for DBP, insignificant for SB) with similar readings MAP, HR and pulse pressure between Day-1 and Day-2. The

nocturnal decline between day-1 and day-2 were 10.2 vs. 8.8 mmHg for SBP and 10.8 vs. 8.6 mmHg for DBP ($p < 0.05$ for DBP, insignificant for SBP). MAP and pulse pressure declined similarly between day 1 and 2 while heart rate did not demonstrate a nocturnal decline in either study days. We found a strong correlation and concordance between day-1 and day-2 regardless of the used method to separate day and night (coefficients all above 0.79 except for HR). (Table-3)

Based on fixed clock separation, eleven subjects (44%) were non-dippers on both days, 6 (24%) were dippers on both days, 3 (12%) were non-dippers on day1 and became dippers on day-2 and 5 (20%) were dippers on day1 and became non-dippers on day2. The ratios were slightly different for asleep:awake separation since 10 patients (40%) were consistent dippers and 8 (32%) patients were consistent no-dippers. Furthermore, there were 2 (8%) reverse-dippers in the non-dipper group (one consistently and the other one inconsistently). Overall, 17/25 (68%) and 18/25 (72%) subjects stayed in the same dipping category based on Day:Night or Asleep:Awake categorizations, while 8/25 (32%) and 7/25 (28%) changed their dipping status (Table4). The Cohen's Kappa coefficient was 0.34 and (ASE= 0.18, two-sided probability of Kappa equal zero = 0.09) for Day:Night ratio and 0.36 for asleep:Awake ratios (ASE=0.178, two sided probability of Kappa equal zero = 0.0473). (See Table-4)

Univariate analyses did not show any significant associations between the dipping consistency (using both night:day and asleep:awake ratios) and eGFR, age, duration of hypertension, SBP or DBP at final titration visit in HALT, urine aldosterone levels, BMI, caffeine consumption, gender, smoking or race (Table-5). When night:day ratios were considered as continuous variables, Pearson correlation coefficients and concordance coefficients were 0.58 and 0.56 for SBP and 0.56 and 0.54 for DBP respectively (Figure-2). The coefficients were higher for SBP and lower for DBP using the awake:asleep ratios. No significant associations with any of the previously reported covariates were found.

Discussion

The increasing use of HBPM requires the questioning of the role of ABPM for non-office based blood pressure monitoring. Advantages of HBPM include cost effectiveness, good prediction of cardiovascular outcomes, strong correlation with daytime ABPM, and the increased compliance with antihypertensive regimens when home monitoring is used [28–30]. The main advantages of ABPM over HBPM include additional blood pressure readings, and insight into the diurnal variations of blood pressure including nocturnal dipping and the early morning surge. Both have both been associated with worse cardiovascular outcomes [31]. The predictive power of nocturnal dipping on cardiovascular outcomes has been established from longitudinal studies, such as the Ohasama study [32] where each 0.05 increment in night:day ratio of SBP or DBP corresponded to a 20% increased risk of cardiovascular death, even when blood pressure was below 135/80.

However, reproducibility of nocturnal dipping in ADPKD has been controversial. Thus far, evidence suggests that ABPM is superior to OBPM in diagnosing masked hypertension and prehypertensive state in ADPKD [33] and positive correlations between average 24 h SBP and LVMI exist in normotensive and hypertensive ADPKD patients (19). Importantly, ADPKD patients also demonstrate lower amplitude of the nocturnal decline and a higher frequency of non-dipping than essential hypertensive patients [21]. Therefore, the significance and reproducibility of non-dipping and the comparative place of ABPM and HBPM are extremely important to establish in this patient population.

Our study is the first to compare two sets of ABPM over a relatively short interval (7–15 days) in a hypertensive (or prehypertensive) ADPKD population with relatively uniform

clinical characteristics and on stable antihypertensive regimens. Of note, all patients were either hypertensive (BP > 130/80) or had been on antihypertensive agents prior to screening visit of the HALT-PKD trial. We confirmed an excellent correlation between mean SBP, DBP, MAP and HR between the two days of measurement and establishes that the majority (56–64%) of our ADPKD patients are non-dippers with a small proportion (8%) demonstrating reverse dipping. Reverse-dipping is typically present in approximately 11% of population with essential hypertension and is associated with a 5 fold increase in cardiovascular mortality compared to dippers [34]. Of note, the frequency of non-dipping in essential hypertension is between 25 and 42% based on a single measurement [35], significantly less than the frequency found in this relatively healthy ADPKD population.

We observed a 68% and 72% consistency rate for nocturnal dipping status based on fixed clock and asleep:awake status. These values are similar to studies in essential hypertension [36] and in contrast with the previously reported 36.6% – 44% (24). Importantly, in previous studies, measurements were obtained over a longer period (12 months) in a heterogeneous ADPKD population with variable hypertension status and changing antihypertensive medication regimens.

We chose the most restrictive definition of dipping (night:day and asleep:awake ratios of both SBP and DBP drops >0.9) since a comparative study showed a slightly better reproducibility rate by using both SBP and DBP when compared to MAP or DBP alone [37]. The lack of uniformity in definitions has been proposed as a possible explanation for lack of reproducibility of the dipping status in many studies [38–39]. Multiple other definitions were considered, however the definitions chosen for this study allows for application to a general ADPKD population and addresses the inherent inter-individual variability of daily life. We compared results using the fixed-hour separation of day and night (06:00 to 21:59 vs. 22:00 to 05:59) with the self reported sleep-awake times and the results were very similar is consistent with the uneventful diaries in the majority of our patients. In addition, by design, we tried to minimize the influence of known factors that may affect the nocturnal dipping (day of the week, antihypertensive medication regimen, lapse of time between the two measurements, severely limited mobility making patients bedridden, and night-shift workers).

We could not identify any associations between dipping status (or consistency of dipping) and reported variables such as race, gender, age, renal function and caffeine intake. This may be due to the small number of participants but could also be due to misclassification error (ratios of night/day BP of 0.8999 vs. 0.901 changed the dipping status) and the unusually low blood pressure targets that were achieved in HALT-PKD trial by using the blockers of the RAAS, where half of patients were additionally assigned to a blood pressure level of <110/75 and the other half to 120–130/70–80 mmHg. We intentionally excluded “blood pressure load” analysis in our study due to the unusually low blood pressure load imposed by the blood pressure targets of the clinical trial [40]. Sample size may directly affect the strength of the presented evidence and also has limited us from using logistic or linear regression models to further elucidate possible explanations for variability of dipping. External validity of our results is limited due to lack of racial diversity and exclusion of advanced renal insufficiency (Chronic kidney disease stages IV and V, eGFR < 25).

Relationship between consistent dipping on at least two occasions or dipping over 48 hours and target organ damage outcomes need to be investigated in ADPKD population since the first pattern has been associated with greater cardiac abnormalities than variable dipping in untreated hypertensive patients [41] and the second demonstrates a dramatic 89% consistency of dipping [42]. Therefore “Double dipping” defined as either consistent

dipping on more than one occasion or over 48 hours, may provide better risk stratification than “single dipping”, and should be investigated in ADPKD population.

Finally, determination of the role of biological factors that may influence day-to-day inconsistency of the dipping status such as urinary sodium excretion [43], neurohormonal regulation of blood pressure sympathetic nervous activity, endothelial dysfunction, dietary factors (ie, potassium intake) and compliance issues with medications should all be considered [44–47].

Conclusions

We conclude that ABPM measurements of SBP, DBP, MAP and HR are strongly reproducible in optimally treated hypertensive (or prehypertensive) ADPKD patients over 7–15 days. Non-dipping is predominant in this population with relatively conserved renal function and an excellent control of blood pressure by using the blockers of the RAAS. Reproducibility of non-dipping is at best moderate. Variability of dipping status may reflect biological changes rather than measurement errors. Future research is warranted to elucidate these factors and also determine an optimal ABPM regimen, including repeated or longer measurements of ABPM, for a better prediction of cardiovascular and renal outcomes in ADPKD.

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Figure-1.
Place of the pilot ABPM study in HALT-PKD trial

Figure-2.
Correlation between night:day ratios and Asleep:Awake ratios of SBP and DBP between Day-1 and Day-2

Table-1

Baseline characteristics

Variables	All patients N=25 Mean (SD)
Gender (% Male)	48%
Race (% Non-African American)	92%
BMI (Kg/m ²)	26.6 (5.1)
Age at baseline (years)	43.1 (8.6)
Age of onset of HTN (years)	33.6(11.1)
Duration of HTN (years)	9.6 (10.6)
eGFR (mL/min/1.73 m ² of BSA)	63.1 (20.5)
Creatinine (mg/dL)	1.29 (0.45)
Smoking (% active smokers)	4%
Caffeine (% drinkers)	76%
Office End-of-titration SBP	113.55 (8.7)
Office End-of-titration DBP	71.7 (8.8)
Serum Potassium (meq/dL)	4.1 (0.36)
Medication (% of patients on <2 meds)	76%
Urine Aldosterone Baseline	9.7 (4.2)
Urine Aldosterone F5	6.9 (5.5)

Table-2

Comparison of Blood pressure readings between day-1 and Day-2 during day and night.

	Day-1						Day-2					
	Day	Night	(Day-Night)	Awake	Asleep	(Awake-Asleep)	Day	Night	(Day-Night)	Awake	Asleep	(Awake-Asleep)
SBP (mmHg)	121.8 (9.6)	110.1 (11.4)	11.7 (10.5)	123 (8.5)	108.7 (11.7)	14.3 (8)	120.4 (10.4)	111.6 (12.5)	8.8(9.5)	122.2 (9.8)	109.8 (12.4)	12.4 (9.2)
DBP (mmHg)	77.6 (8.4)	66.8 (8.8)	10.8 (7.3)	78.5 (8.0)	66.7 (9)	12.83 (6)	77.1 (9.1)	68.5 (8.8)	8.6(8.3)	78.1 (8.9)	67 (9.8)	11.2 (7.9)
MAP (mmHg)	92 (8.4)	80.9 (10.8)	11.1 (7.2)	93.3 (7.4)	79.7 (9.3)	13.5 (6.8)	91.6 (9)	83.3 (9)	8.3 (8.6)	92.9 (8.7)	81.7 (10.3)	11.2 (8.3)
HR (Beats/min)	73 (10.8)	61.7 (9.9)	11.3 (7.2)	74 (10.6)	59.7 (9.8)	14.4 (6.5)	71.6 (9.5)	63.8 (11.2)	7.9 (7.4)	72.5 (9.3)	61.4 (11.2)	11.1 (7.9)
P (mm Hg)	44.3 (6.4)	43.4 (7.3)	0.9 (4.2)	44.6 (6.5)	43.1 (7.2)	1.5 (4.4)	43.3 (7)	43 (5.9)	0.3 (4.4)	44 (6.9)	42.7 (6.7)	1.3 (4.5)

SBP : Systolic Blood Pressure DBP: Diastolic Blood pressure MAP: Mean Arterial Pressure HR: Heart rate PP: Pulse Pressure

Note: No statistically significant difference between individual values of each parameter at Day-1 and Day-2.

Table-3

Correlation and concordance coefficients between day-1 and day-2 Night:Day and Asleep:Awake Ratios.

	Correlation coefficients				Concordance coefficients			
	Day	Night	Awake	Asleep	Day	Night	Awake	Asleep
SBP	0.89	0.79	0.88	0.88	0.88	0.78	0.87	0.87
BP	0.91	0.81	0.91	0.85	0.91	0.80	0.90	0.85
MAP	0.91	0.82	0.90	0.84	0.91	0.78	0.89	0.82
HR	0.79	0.73	0.80	0.75	0.78	0.71	0.78	0.73
PP	0.87	0.85	0.89	0.90	0.86	0.83	0.88	0.90

SBP : Systolic Blood Pressure DBP: Diastolic Blood pressure MAP: Mean Arterial Pressure HR: Heart rate PP: Pulse Pressure

Dipping status, Day-1 and Day-2

	Fixed clock separation of Day and Night			Sleep Awake separation		
	Non-Dippers (n %)	Dippers (n %)	Total (n %)	Non-Dippers (n %)	Dippers (n %)	Total (n %)
Day-2						
Non dippers	11 (44%)	3 (12%)	14 (56%)	10 (40%)	3 (12%)	13 (52%)
Dippers	5 (20%)	6 (24%)	11 (44%)	4 (20%)	8 (32%)	12 (48%)
Total	16 (64%)	9 (36%)	25 (100%)	14 (56%)	11 (44%)	25 (100%)

Cohen's Kappa statistics= 0.34 (Asymptotic Standard Error =0.188) Two sided p-value = 0.087

Cohen's Kappa statistics= 0.38 (Asymptotic Standard Error=0.179) Two sided P-value = 0.047

Table-5

Univariate analysis evaluating consistency of dipping status at Day-1 and Day-2 and potential predictor variable.

Variable	Fixed clock Day and Night separation			Asleep-Awake separation		
	Inconsistent dipping Mean (SD) n=8	Consistent dipping Mean (SD) n=17	p value	Inconsistent dipping Mean (SD) n=7	Consistent dipping Mean (SD) n=18	p value
Creatinine (mg/dl)	1.47 (0.54)	1.2 (0.39)	0.40 ^W	1.53 (0.48)	1.19 (0.4)	0.13 ^W
Sex (% females)	37.5 %	58%	0.41 ^F	40%	61%	0.20 ^F
Race [*] (% of Caucasians)	75%	100%	0.09 ^F	14.2%	100%	0.07 ^F
eGFR (ml/min/1.72 m2)	58.39 (25.49)	65.28 (18.09)	1 ^W	54.60 (18.8)	66.4 (20.6)	0.27 ^W
Duration of HTN (years)	8.88 (9.96)	9.88 (11.11)	0.42 ^W	9.29 (10.7)	9.7 (10.8)	0.81 ^W
Age (years)	45 (5.4)	42.24 (9.71)	0.68 ^W	44.4 (5.6)	42.6 (9.5)	0.93 ^W
Baseline Office SBP (mmHg)	115.6 (7.6)	112.52 (9.31)	0.35 ^W	115.6 (4.4)	112.7 (9.9)	0.62 ^W
Baseline Office DBP (mmHg)	74.6 (5.96)	70.24 (9.77)	0.43 ^W	70.8 (9.8)	72.1 (8.7)	0.70 ^W
BMI (kg/cm2)	29.9 (1.89)	24.89 (5.41)	0.55 ^W	27.6 (3.9)	26.1 (5.6)	0.59 ^W
Medication (step doses)	3.5 (2.07)	2.47 (1.74)	0.89 ^W	3.4(1.7)	2.6 (1.9)	0.40 ^F
Caffeine drinkers (%)	87.5%	76%	1 ^F	71.4 %	72.2 %	0.69 ^F
Smokers (%) ^{**}	0%	6%	0.41 ^F	0%	0.6 %	0.73 ^F
Baseline U-Aldosterone (ng/ml)	7.34 (7.8)	6.75 (4.31)	1 ^W	4.2 (1.8)	8 (6)	0.13 ^W
Serum Potassium (mEq/l)	4.23 (0.39)	4.06 (0.34)	0.22 ^W	3.42 (0.4)	4.1(0.33)	0.62 ^W

eGFR: estimated Glomerular Filtration Rate HTN: Hypertension U-Aldosterone: Urinary Aldosterone SBP: systolic Blood Pressure DBP: diastolic Blood pressure BMI: Body Mass Index

^F Fisher's exact test

^W Wilcoxon's sum rank test

^{*} Only 2 African-Americans

^{**} Only one non-smoker

Table-6

Correlation coefficients for night:day and asleep:awake ratios between Day-1 and Day-2

Variable	Mean (SD)	Correlation Coefficient (Pearson)	Concordance Coefficient
SBP N:D-Day-1	0.905 (0.079)	0.58	0.56
SBP N:D-Day-2	0.928 (0.081)		
(SBP N:D- Day-1) – (SBP N:D-Day2)	–0.023 (0.073)		
DBP N:D-Day-1	0.863 (0.096)	0.56	0.53
DBP N:D-Day-2	0.891 (0.112)		
(DBP N:D- Day-1) – (DBP N:D-Day2)	–0.028 (0.099)		
SBP A:A-Day-1	0.884 (0.069)	0.69	0.67
SBP A:A-Day-2	0.899 (0.076)		
(SBP A:A-Day-1) – (SBP A:A-Day2)	–0.015 (0.057)		
DBP A:A-Day1	0.837 (0.077)	0.48	0.45
DBP A:A-Day-2	0.860 (0.104)		
(DBP A:A-Day-1) – (DBP A:A-Day2)	–0.023 (0.095)		

DBP: Diastolic Blood Pressure SBP: Systolic Blood Pressure N:D: Night:Day A:A: Asleep:Awake