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Proteinuria and Nocturnal Blood Pressure Dipping in Hypertensive Children and Adolescents

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Abstract

Background: Absence of nocturnal blood pressure dipping is associated with adverse cardiovascular outcomes in adults, and proteinuria is a risk factor for non-dipping in this population. Risk factors for non-dipping in children are largely unknown.

Methods: We retrospectively identified patients aged 5 to 19 years who underwent 24-hour ambulatory blood pressure monitoring (ABPM) from August 2018 to January 2019 and had a spot urine protein to creatinine ratio (PCR) within one year of their ABPM. Dipping was defined as ≥10% reduction in systolic and diastolic blood pressure from day to night. Multivariable logistic and linear regression models evaluated the association of proteinuria with non-dipping.

Results: Among 77 children identified, 27 (35.1%) were non-dippers. Each two-fold higher urine PCR was associated with 38% higher odds of non-dipping, after adjusting for body mass index (BMI). Higher urine PCR was also associated with a lower diastolic dipping percentage by 1.33 (95% CI 0.31 to 2.34), after adjusting for BMI, age, and estimated glomerular filtration rate.

Conclusion: Limitations of this study include its retrospective design and the time lapse between urine PCR and ABPM. Proteinuria appears to be associated with blood pressure non-dipping in children. This finding needs to be confirmed in prospective studies.

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Category of Study: Clinical Research Article

Consent: This retrospective, cross-sectional study was approved by the UCSD IRB (#200336). Consent was not required.

Disclosures: none.

Introduction:

Along with the rising prevalence of hypertension in children, there has been a concomitant increase in the use of 24-hour ambulatory blood pressure monitoring (ABPM) for diagnosis and treatment (1, 2). Twenty-four hour ABPM allows for the dynamic assessment of blood pressure including at nighttime (3). In otherwise healthy children being evaluated for hypertension using ABPM, approximately 14% are found to lack the expected lower blood pressure at night, defined as “non-dippers” (3). The prevalence of non-dipping is much higher at 39% in children with chronic kidney disease (CKD) (4). The exact pathophysiology of non-dipping remains unclear; however, non-dipping has been associated with increased nocturnal natriuresis(5).

In adults, absence of nocturnal blood pressure dipping is associated with adverse cardiovascular outcomes, including increased left ventricular hypertrophy and mortality (6, 7). In young adults who were followed for ten years, inadequate systolic dipping was significantly associated with future subclinical coronary artery atherosclerosis (8). This is particularly important in pediatric populations, where few manifest clinical evidence of cardiovascular disease (CVD), yet identifying children at risk for future CVD may provide opportunities for primary prevention. Risk factors for non-dipping in adults include obesity, obstructive sleep apnea, and proteinuria (9–11). In children, prior studies identified obesity as a risk factor for non-dipping, but the relationship between proteinuria and non-dipping is unknown (3, 12–14). Thus, the goal of this study was to describe the relationship between proteinuria and nocturnal non-dipping on 24-hour ABPM in children. Based on findings in adults, we hypothesized that greater proteinuria would be associated with nocturnal non-dipping in children, independent of obesity, kidney function, and other shared risk factors.

Methods:

Data Source

We conducted a retrospective, cross-sectional study in which we identified consecutive subjects aged 5 to 19 years who underwent 24-hour ABPM at Rady Children’s Hospital in San Diego from August 2018 to January 2019. The study was approved by the Institutional Review Board at the University of California San Diego Health System (#200336).

Subject Selection/Methods

Subjects were included if they had either a urine protein or urine microalbumin and urine creatinine measurement within one year of their ABPM study. Exclusion criteria included age ≥ 20 years, inadequate ABPM study by which to define dipping patterns, as determined by the interpreting physician based on AHA criteria (1), as well as any known genetic tubular disease. Subjects underwent 24-hour ABPM either as part of the evaluation for elevated blood pressure or for assessment of blood pressure control on anti-hypertensive therapy. Through chart review, we collected information including: age, sex, race, past medical history, birth history, prior diagnosis of hypertension, and current anti-hypertensives at time of the ABPM. We also obtained the serum creatinine of closest proximity in timing to ABPM (within three years), and cardiac geometry data of closest proximity in timing

to ABPM by echocardiography (within two years), including left ventricular mass index (LVMI in $g/m^{2.7}$) and presence of left ventricular hypertrophy (LVH).

Among the subset with missing urine protein to creatinine ratio (PCR), but available urine albumin and creatinine measurements (N=7, 9.1%), we used the equation of Weaver et al. to transform the urine albumin to creatinine ratio to a urine PCR (15).

All ABPM studies were performed using a Spacelabs (Snoqualmie, WA) 90217 or 90227 monitor. The monitors had been placed by our trained medical assistants or nursing staff at the time of the clinic visit. The appropriate cuff size was determined based on the "Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents" by the American Academy of Pediatrics (2). The monitor cycles every 20 minutes during wake times and every 30 minutes during sleep to provide blood pressure readings. Patients and their families were asked to document an activity log, including sleep and wake times.

Dipping was defined as ≥10% reduction in mean systolic and diastolic blood pressure from day to night (1, 2). Ambulatory hypertension was defined as a mean systolic or diastolic blood pressure ≥ 95^{th} percentile for age, sex, and height during either the awake or sleep period, with all loads between 25 to 50% (1, 16). Severe ambulatory hypertension was defined as a mean systolic or diastolic blood pressure ≥ 95^{th} percentile for age, sex, and height during either the awake or sleep period, with at least one load > 50%. Prehypertension was defined as a mean ambulatory blood pressure < 95^{th} percentile for age, sex, and height, with loads ≥ 25% (1, 16). Mean systolic and diastolic 24-hour indices were calculated by dividing the mean 24-hour systolic or diastolic blood pressure by the 95^{th} percentile for sex and height. LVH was defined as LVMI ≥ 95^{th} percentile for age and sex (17). Estimated glomerular filtration rate (eGFR) for subjects less than 18 years of age was calculated by both the original Schwartz (Schwartz I) and bedside-Schwartz (Schwartz II) equations (18, 19). Because cystatin C was unavailable in the majority of subjects, we were unable to calculate eGFR based on the creatinine-cystatin C based CKiD equation. For subjects 18 years of age and older, eGFR was calculated by the Modification of Diet in Renal Disease (MDRD) 4-variable equation (20). A diagnosis of CKD was assigned based on ICD-10 code, as documented in the electronic medical record.

Statistical Analysis

Continuous variables were described as mean ± standard deviation. Means were compared using Independent Samples t-test. Categorical variables were described by frequency and percent. Categorical variables were compared using Pearson Chi-Squared tests. Urine PCR (mg/mg) was $\log_2$ – transformed to normalize the data. For our primary outcome of non-dipping, we utilized multivariable logistic regression models with the exposure of interest being $\log_2$(PCR). We evaluated unadjusted and mutually adjusted models. Variables that were considered for adjustment included age, sex, BMI (kg/m^2), and eGFR (Schwartz I or MDRD). We then employed backwards selection to retain important confounders in a final model, with a p-value threshold for inclusion of < 0.2. In secondary analysis, we evaluated the association of $\log_2$(PCR) with systolic and diastolic dipping (%) in multivariable linear regression models. Similarly, we employed backwards selection to retain important

confounders. A p-value of < 0.05 was considered significant. All statistical analyses were performed using IBM SPSS version 26 (Armonk, NY).

Results

General Characteristics of Subjects

A total of 214 ABPM studies were completed between August 2018 and January 2019. Of these, one was a repeat ABPM on the same subject, and one subject with Lowe Syndrome was excluded (tubular proteinuria). Twenty ABPMs were classified as inadequate quality by the interpreting physician. Of the remaining 192, seventy-seven had a urine protein or urine microalbumin test within one year of the ABPM and were included in the study (Figure 1). Two subjects had glomerular disease, one with IgA nephropathy and one with IgM nephropathy and nephrotic syndrome. Two subjects had secondary hypertension from Takayasu's arteritis. The median time between ABPM and urine PCR was 25 days (IQR −25 to +48), between ABPM and echocardiogram was 42 days (IQR −50 to +331) and between ABPM and serum creatinine was 22 days (IQR −61 to +114).

The mean age of subjects was 14.2±3.5 years. Females comprised 35.1% of the cohort. Nearly 57% of subjects were Hispanic and 5% were African American. The mean 24-hour systolic blood pressure was 116.1±13.2 mmHg. The mean 24-hour systolic blood pressure index was 0.92±0.1. Mean eGFR (by Schwartz I or MDRD) was 152±36.3 ml/min/1.73m2, and median urine PCR was 0.07 [IQR 0.04, 0.12] mg/mg creatinine.

Among the 77 subjects, 27 were classified as non-dippers (35.1%). There were no significant differences in age, sex, race, anti-hypertensive use, or eGFR between dippers and non-dippers (Table 1). There was a trend towards higher BMI (mean difference 2.7 kg/m^2, 95% CI −0.41 to 5.84) and higher log_2(PCR) in non-dippers (mean difference 0.77, 95% CI −0.08 to 1.60). Non-dippers had a significantly higher LVMI (mean difference 6.9 $g/m^{2.7}$, 95% CI 1.6 to 12.2) and significantly more LVH (30.4% vs. 5.1%, p = 0.01), as compared to dippers. There were no differences between dippers and non-dippers in regard to clinic blood pressure measurements.

Proteinuria and Non-Dipping

The distribution of log_2(PCR) by dipping status is shown in Figure 2. The distribution was right skewed in non-dippers. Age, sex, eGFR, and blood pressure medication use were not found to be significant confounders in the analysis (p > 0.2). After backwards selection, only log_2(PCR) and BMI were retained as covariates. In a model simultaneously adjusting for these two variables, a two-fold higher urine PCR was associated with 38% higher odds of non-dipping (1.38, 95% CI 1.01 to 1.88) and a 5 kg/m^2 higher BMI was associated with 54% higher odds of non-dipping (1.54, 95% CI 1.00 to 2.29) (Table 2).

In the secondary analysis, a two-fold higher urine PCR was associated with a lower systolic dipping percentage by 0.72 (95% CI 0.002 to 1.44), after adjustment for BMI and sex (Table 3). Similarly, a two-fold higher urine PCR was associated with a lower diastolic dipping percentage by 1.33 (95% CI 0.31 to 2.34), after adjustment for BMI, age, and eGFR (Table 3). A grouped scatterplot of the correlation between systolic dipping percent

and $\log_2$(PCR) and diastolic dipping percent and $\log_2$(PCR) is shown in Figure 3. Diastolic dipping percentage appeared to associate more strongly with proteinuria than did systolic dipping percentage.

Discussion

We demonstrate that greater proteinuria is associated with non-dipping status in children who completed 24-hour ABPM for either evaluation of elevated blood pressure or continued management of hypertension. Additionally, our data corroborates prior studies showing that a higher BMI is associated with non-dipping (3, 14). If associations in children mimic those seen in adults, then non-dipping on ABPM may identify children at higher risk for CKD progression and future CVD. Thus, identifying risk factors such as proteinuria may allow clinicians to better recognize children who may benefit from serial ABPM monitoring and more aggressive primary prevention strategies.

While little is known about non-dipping in children, it is known to be associated with adverse clinical outcomes in adults. In participants of the Jackson Heart Study, reverse dipping (higher systolic blood pressure at night than day) was associated with increased LVMI and higher prevalence of LVH, even after adjustment for mean daytime systolic blood pressure (21). Similar findings have been demonstrated in adult hemodialysis populations (22). Non-dipping has also been associated with more rapid decline in kidney function in adults (23). Data pertaining to blood pressure dipping and its association with adverse clinical outcomes in the pediatric population is more limited. In a longitudinal study of adolescents with Type 1 diabetes mellitus, non-dipping was associated with hyperfiltration at a two year follow-up (24). In a small cross-sectional study of children with chronic kidney disease, lower systolic blood pressure dipping was associated with lower eGFR (25). Non-dipping has also been associated with surrogate CVD biomarkers in children. An abnormal dipping pattern was associated with increased likelihood of LVH in children with stage 3 to 5 CKD (26). Additionally, in a cross-sectional study of healthy children, dipping patterns were a significant determinant of pulse wave velocity, independent of BMI and other risk factors (27, 28). In twenty subjects with pediatric-onset systemic lupus erythematosus, isolated blood pressure non-dipping was associated with endothelial dysfunction and greater intima-media thickness (29). We add to these studies by demonstrating that proteinuria is associated with non-dipping in hypertensive children and adolescents. This is important as the identification of children with non-dipping may allow for early intervention, as dipping patterns may be modifiable. In adults, adjustment of timing of anti-hypertensive medication from morning to evening resulted in lower nighttime blood pressure, improved overall 24-hour blood pressure, and reduced proteinuria (30, 31). In a trial of adults with CKD and hypertension, nighttime dosing of at least one anti-hypertensive medication significantly reduced risk of CVD at 5 year follow up (32). Recently, a pilot study in pediatric kidney transplant recipients demonstrated that addition of a short-acting blood pressure medication in the evening increased systolic dipping and restored normal dipping profile in 53% of non-dippers who received the intervention (33). Although this study only included transplant patients, and evaluated additive therapy, it demonstrates that nocturnal dipping is modifiable in children. Thus, non-dipping is a modifiable risk factor for CVD, at least in adults, and further studies are needed to determine if it is in the pediatric population as well. Adjustment

of timing of anti-hypertensive therapy provides a feasible intervention that may induce normal dipping profiles in children, and larger, randomized controlled trials in the pediatric population are needed to determine if this will translate into improved clinical outcomes.

A clear understanding of the risk factors associated with non-dipping is important in identifying patients who would benefit from 24-hour ABPM. In adults with resistant hypertension, microalbuminuria was more strongly associated with elevated nighttime systolic blood pressure than with any other office or 24-hour ABPM parameter (34). Likewise, a study by Afsar et al. evaluated 24-hour urinary albumin excretion (UAE) rates in hypertensive adults and found that non-dippers had higher UAE (35). Interestingly, those with both systolic and diastolic non-dipping had higher UAE than those with isolated systolic or diastolic non-dipping. Fewer studies have been done in children evaluating the association of proteinuria with non-dipping, and existing studies are limited to children with diabetes. In a prospective study that followed adolescents with Type 1 diabetes mellitus, an increase in nocturnal systolic pressure was significantly associated with the development of microalbuminuria during follow-up (36). Only six of our participants had diabetes. Thus, to our knowledge, our study is the first to investigate the association of proteinuria with non-dipping in a more general pediatric cohort referred for evaluation of elevated blood pressure.

The pathophysiology of abnormal diurnal variation of blood pressure is not well understood, though a number of pathways might play a role. Overactivation of the sympathetic nervous system, an abnormal hormone profile (elevated catecholamines, renin, or aldosterone), and high dietary sodium load have all been proposed as potential mediators of this phenomenon (37). The mechanism underlying the association between proteinuria and non-dipping is similarly unclear. We hypothesize that proteinuria may identify persons with impaired excretion of daytime dietary sodium load. A decrease in the ability to effectively excrete sodium may lead to elevated nocturnal blood pressure as a compensation mechanism to enhance natriuresis overnight, if insufficient sodium is excreted during the daytime hours (38). This hypothesis requires further investigation.

Our study has important limitations. First, the sample size is small which limits the statistical power to capture more subtle differences in demographics between dippers and non-dippers. Nonetheless, this study is relatively large compared to other ABPM studies in pediatric populations. Second, the cross-sectional design of our study prevents us from making any interpretations about causality. Third, the urine PCR was obtained within one year of ABPM date; given the time lapse between collection of these data, there is potential for misclassification. Such misclassification would likely be non-differential with respect to dipping patterns, and thus would likely bias the results towards the null hypothesis. Additionally, given the retrospective design of the study, we do not have serial measurements of urine PCR for each subject or data from 24-hour urine collections, which is a source of information bias. Further prospective studies with simultaneous ABPM and 24-hour urine protein collections are needed. Fourth, because of the nature of our question, we selected only subjects who had obtained either a urine protein or urine microalbumin test and included only children who were referred for ABPM measurements at our academic pediatric hospital, resulting in selection bias. Finally, our cohort is 57% Hispanic so

generalizability to other populations is limited, and results should be confirmed in other settings.

In conclusion, greater proteinuria is associated with non-dipping status in children. Prospective studies are needed to further delineate this relationship and allow for a better understanding of the pathophysiology. Given the significant impact of non-dipping on clinical outcomes in adults, the finding that non-dipping may be modifiable, and such modifications translate into lower risk of CVD and mortality in adults, there is an urgent need to identify additional risk factors for non-dipping, its associations with clinical outcomes, and its ability to be modified in children. As both abnormal dipping patterns and higher urine PCR are strongly associated with adverse outcomes in adults, our results suggest that children found to have non-dipping should be evaluated with a urine PCR, and, conversely, those with proteinuria may benefit from 24-hour ABPM evaluation.

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Impact Statement:

- Our study demonstrates the association of proteinuria with non-dipping of blood pressure in children.
- This association has been explored in adults, but to our knowledge, this is the first time it is evaluated in children referred for evaluation of elevated blood pressure.
- Non-dipping is a modifiable risk factor for kidney function decline and cardiovascular disease in adulthood, and thus early identification in children is important. The association between proteinuria and non-dipping in children will allow us to more readily identify those at risk, with a future focus on interventions to modify blood pressure dipping patterns.

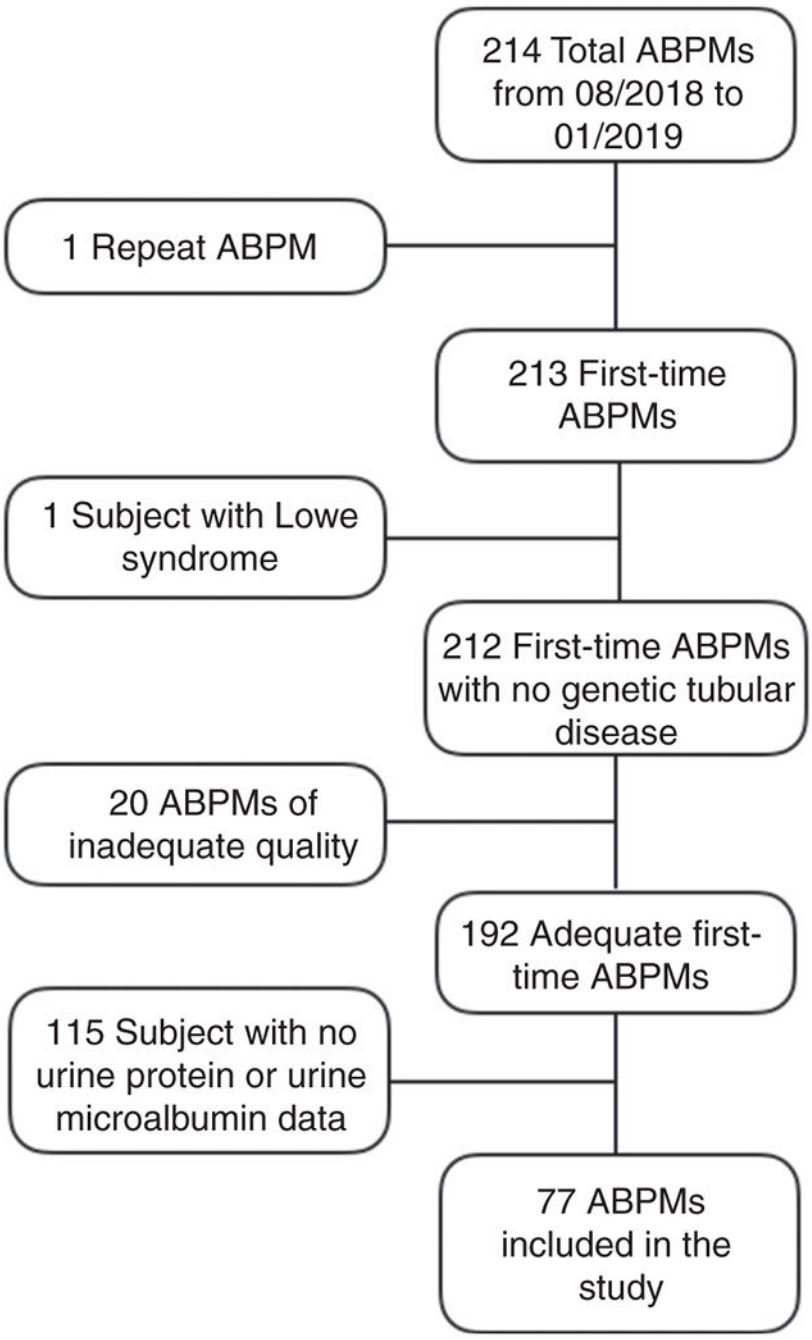

Figure 1.

A total of 214 ABPMs were completed between August 2018 and January 2019, of which 213 were first-time ABPMs. One subject had Lowe Syndrome and was excluded. Twenty ABPMs were of inadequate quality to be interpretable. Of the remaining 192, seventy-seven had a urine protein or urine microalbumin test and were included in the study.

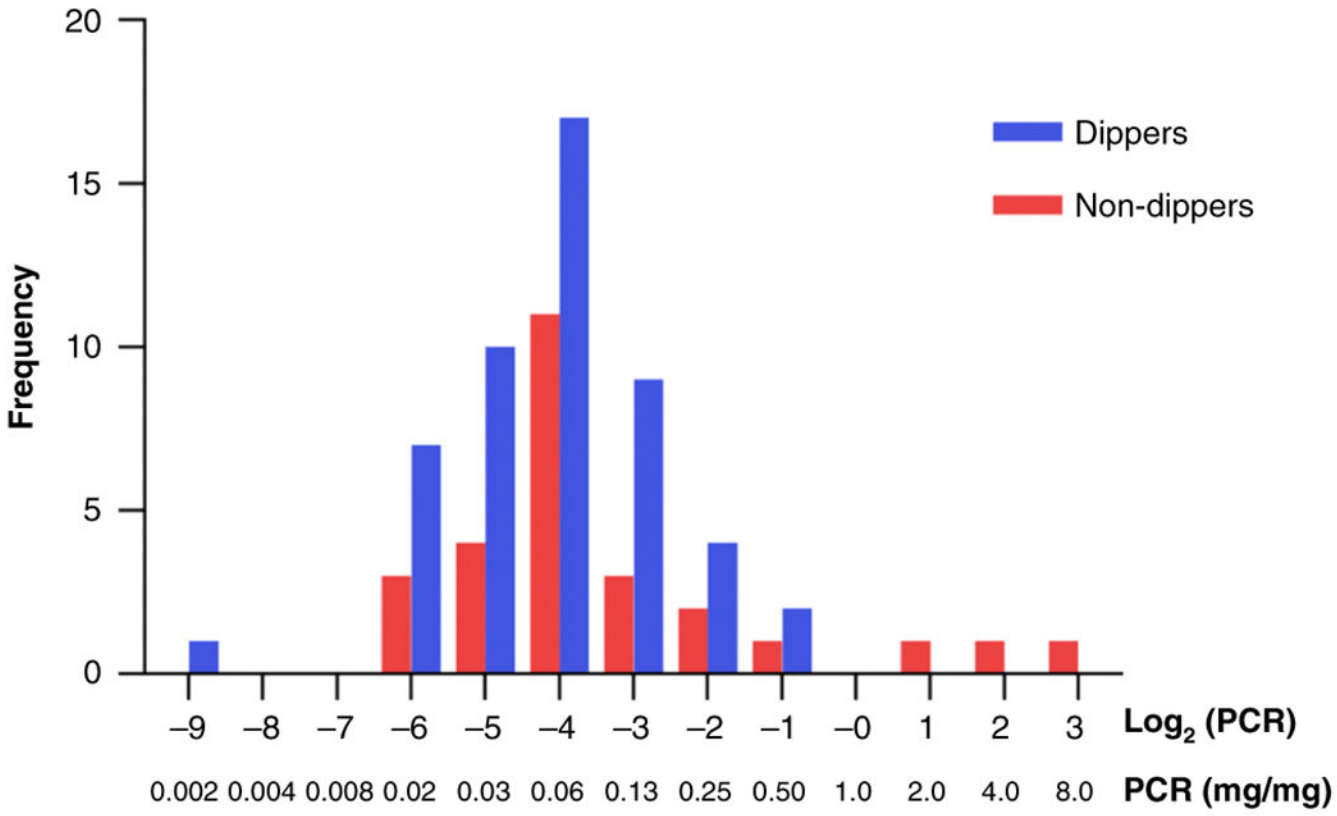

Figure 2.
The distribution of $\log_2$(urine protein/creatinine) in dippers (blue) and non-dippers (red).

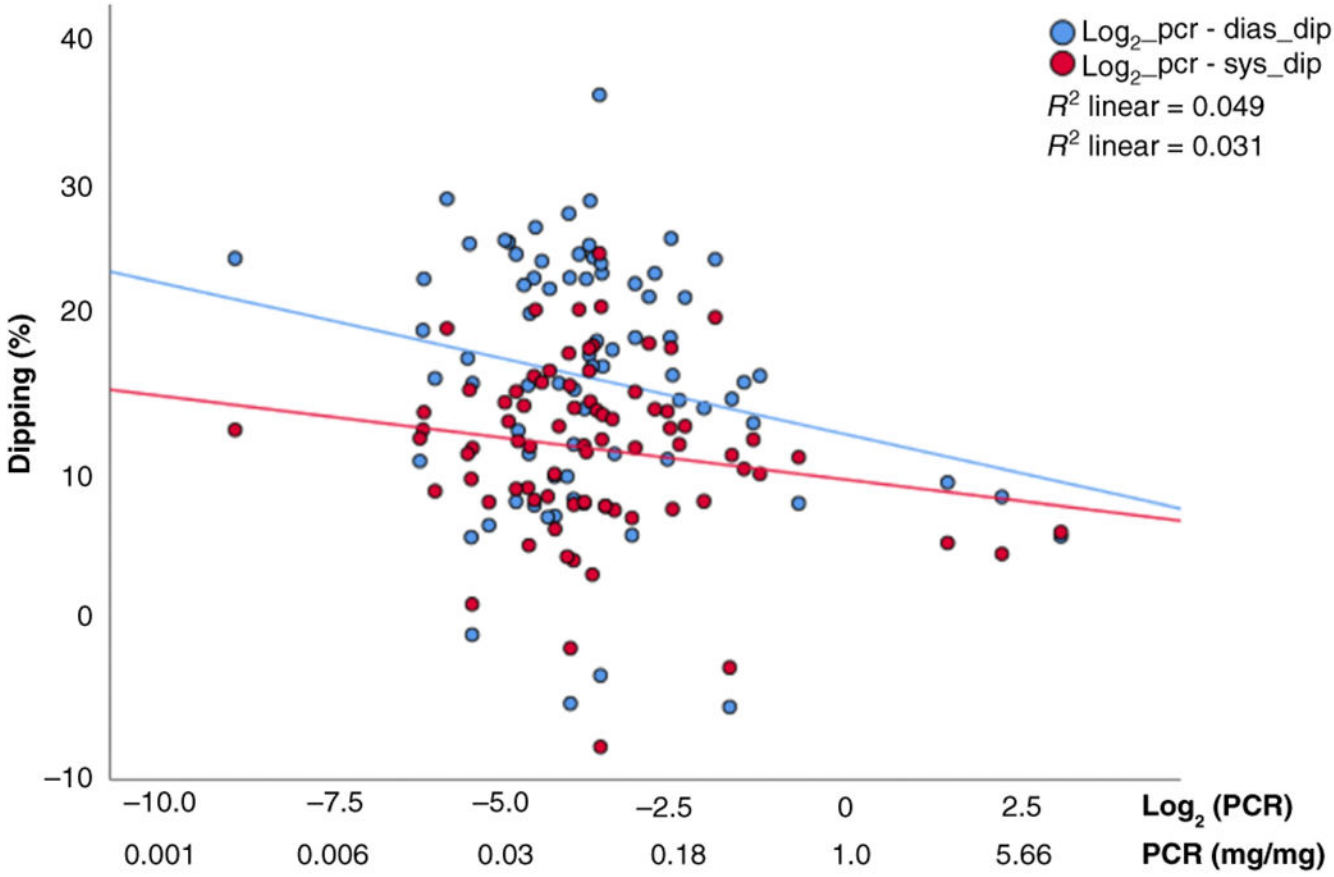

Figure 3.

Grouped scatterplot of the correlation between diastolic dipping percentage and $\log_2$(urine protein/creatinine) shown in blue, and systolic dipping percentage and $\log_2$(urine protein/creatinine) shown in red.

Table 1.

Baseline characteristics of subjects by dipping status.

	Overall N = 77	Dipper N = 50	Non-Dipper N = 27	p-value
Age (years)	14.2 (3.5)	14.0 (3.6)	14.6 (3.3)	0.44
Female (%)	27 (35.1)	16 (32.0)	11 (40.7)	0.44
Race (%)				0.31
White	18 (23.4)	13 (26.0)	5 (18.5)	
Hispanic	44 (57.1)	25 (50.0)	19 (70.4)	
African American	4 (5.2)	4 (8.0)	0 (0)	
Asian	5 (6.5)	3 (6.0)	2 (7.4)	
Other	6 (7.8)	5 (10.0)	1 (3.7)	
Overall anti-hypertensive use (%)	19 (24.7)	10 (20.0)	9 (33.3)	0.20
ACE inhibitor/ARB use (%)	8 (10.4)	5 (10)	3 (11.1)	0.44
Prematurity (%), n=61	7 (11.5)	5 (11.9)	2 (10.5)	0.88
Body Mass Index (kg/m^2)	25.3 (6.7)	24.4 (6.2)	27.1 (7.3)	0.09
Body Mass Index, z-score	1.1 (1.0)	1.0 (0.9)	1.3 (1.2)	0.26
Log_2(urine protein to creatinine in mg/mg)	−3.8 (1.8)	−4.0 (1.4)	−3.3 (2.3)	0.07
Left Ventricular Mass Index ($g/m^{2.7}$), n = 53	34.8 (9.9)	32.1 (7.1)	39.0 (12.2)	**0.01**
Left Ventricular Hypertrophy (%), n = 62	9 (14.5)	2 (5.1)	7 (30.4)	**0.01**
Chronic Kidney Disease (%)	10 (13.0)	4 (8.0)	6 (22.2)	0.08
Schwartz I or MDRD eGFR (ml/min/1.73 m^2)	152 (36.3)	156 (32.1)	145 (42.6)	0.20
Schwartz II eGFR (ml/min/1.73 m^2), n= 69	105 (25.6)	104 (24.6)	106 (28.3)	0.81
ABPM Category (%)				**0.01**
White Coat	25 (32.5)	20 (40.0)	5 (18.5)	
Prehypertension	19 (24.7)	13 (26.0)	6 (22.2)	
Ambulatory	15 (19.5)	11 (22.0)	4 (14.8)	
Severe Ambulatory	18 (23.4)	6 (12.0)	12 (44.4)	
Systolic Dipping (%)	12.9 (5.9)	16.1 (3.5)	6.8 (4.6)	**<0.001**
Diastolic Dipping (%)	17.7 (8.6)	22.5 (5.4)	8.9 (6.2)	**<0.001**
24-hour Mean SBP (mmHg)	116.1 (13.2)	113.5 (11.5)	120.9 (15.1)	**0.02**
24-hour Mean SBP index	0.92 (0.1)	0.90 (0.1)	0.96 (0.1)	**0.01**
24-hour Mean DBP (mmHg)	69.2 (8.3)	67.4 (8.0)	72.6 (7.9)	**0.01**

	Overall N = 77	Dipper N = 50	Non-Dipper N = 27	p-value
24-hour Mean DBP index	0.90 (0.1)	0.88 (0.1)	0.94 (0.1)	**0.01**
Last office SBP (mmHg)	130.7 (15.4)	129.1 (15.0)	133.7 (15.9)	0.21
Last office SBP, percentile	90.8 (12.2)	89.8 (13.4)	92.8 (8.9)	0.35
Last office DBP (mmHg)	76.0 (10.1)	76.0 (10.5)	75.8 (9.7)	0.93
Last office DBP, percentile	79.9 (20.0)	79.7 (21.1)	80.1 (17.7)	0.94

Table 2.

Association of Log_2 (PCR) with Non-Dipping.

	Unadjusted OR (95% CI)	**Mutually Adjusted[a] OR (95% CI)**	**Backward Selection[b] OR (95% CI)**
Log_2 (PCR)	1.28 (0.97, 1.69)	1.35 (0.97, 1.87)	1.38 (1.01, 1.88)
p-value	**0.086**	**0.074**	**0.041**
BMI (per 5 kg/m^2)	1.34 (0.95, 1.14)	1.69 (1.00, 2.82)	1.54 (1.00, 2.29)
Age (per year)	1.06 (0.92, 1.22)	0.93 (0.77, 1.13)	
Female	1.46 (0.55, 3.86)	0.90 (0.30, 2.70)	
eGFR (per ml/min/1.73 m^2)	0.99 (0.98, 1.01)	0.99 (0.98, 1.01)	
BP medication use	2.00 (0.69, 5.76)	1.58 (0.49, 5.08)	

Abbreviations: PCR, urine protein/creatinine; BMI, body mass index; eGFR, estimated glomerular filtration rate; BP, blood pressure; CI, confidence interval; OR, odds ratio.

[a]Adjusted for all variables including BMI, age, gender, Schwartz I or MDRD eGFR, and BP medication use.

[b]Backward selection model leads to adjustment for BMI only.

P-values reported are for log2(PCR) in the model.

Table 3.

Association of Log_2 (PCR) with Systolic and Diastolic Dipping (%).

	Unadjusted β (95% CI)	Mutually Adjusted[a] β(95% CI)	Backward Selection[b] β(95% CI)
Systolic Dipping			
Log_2 (PCR)	−0.58 (−1.33, 0.16)	−0.68 (−1.43, 0.07)	−0.72 (−1.44, −0.002)
p-value	**0.123**	**0.074**	**0.049**
BMI (per 5 kg/m^2)	−1.50 (−2.45, −0.55)	−1.95 (−3.10, −0.75)	−1.60 (−2.55, −0.65)
Female	−2.86 (−5.62, −0.10)	−1.64 (−4.39, 1.12)	−1.91 (−4.56, 0.74)
Age (per year)	−0.19 (−0.58, 0.20)	0.25 (−0.22, 0.71)	
eGFR (per ml/min/1.73 m^2)	0.02 (−0.02, 0.06)	0.01 (−0.03, 0.05)	
BP medication use	−1.75 (−4.87, 1.36)	−0.58 (−3.61, 2.46)	
Diastolic Dipping			
Log_2 (PCR)	−1.06 (−2.13, 0.02)	−1.16 (−2.23, −0.09)	−1.33 (−2.34, −0.31)
p-value	**0.054**	**0.034**	**0.011**
BMI (per 5 kg/m^2)	−1.95 (−3.40, −0.55)	−3.10 (−4.80, −1.40)	−3.20 (−4.90, −1.55)
Age (per year)	−0.09 (−0.66, 0.48)	0.66 (−0.01, 1.33)	0.65 (−0.01, 1.30)
eGFR (per ml/min/1.73 m^2)	0.03 (−0.02, 0.08)	0.03 (−0.02, 0.09)	0.04 (−0.02, 0.09)
Female	−3.44 (−7.49, 0.61)	−1.22 (−5.17, 2.73)	
BP medication use	−3.20 (−7.70, 1.31)	−1.69 (−6.04, 2.65)	

Abbreviations: PCR, urine protein/creatinine; BMI, body mass index; eGFR, estimated glomerular filtration rate; BP, blood pressure; CI, confidence interval.

[a]Adjusted for all variables including BMI, age, gender, Schwartz I or MDRD eGFR, and BP medication use.

[b]Backward selection model for outcome systolic dipping leads to adjustment for BMI and gender. Backward selection model for outcome diastolic dipping leads to adjustment for BMI, age, and eGFR.

P-values reported are for log_2(PCR) in the model.