Nocturnal Non-dipping Blood Pressure Profile in Black Normotensives Is Associated with Cardiac Target Organ Damage

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Purpose: A non-dipping pattern of nocturnal blood pressure in hypertensive patients is an established predictor of cardiovascular risk, especially in Blacks. However, data on non-dipping normotensives and cardiovascular risk in this population is sparse. In this study, we aim to determine if a non-dipping profile in a cohort of Black normotensives is associated with cardiac target organ damage.

Methods: We studied ambulatory blood pressure patterns in 43 normotensive Black patients of Caribbean origin and classified their profiles as dippers (DP) and non-dippers (NDP) based on their nocturnal blood pressure profiles. Cardiac target organ damage was estimated from 2-D echocardiogram.

Results: The mean age of the cohort was 52 years. Both groups were similar with respect to baseline age, sex, weight, height, body mass index and daytime ambulatory BP. There was a statistically significant difference in nocturnal blood pressure between DP and NDP groups (112 ± 7/64 ± 2 mm Hg vs 117 ± 3/69 ± 2 mm Hg, P=.004). The NDP cohort showed evidence of cardiovascular target damage on echocardiography with a significantly increased relative wall thickness (.35 ± .07cm vs .42 ± .05 cm, P=.001), left ventricular mass index (95 ± 14 vs 105 ± 14 g/m2, P=.018) and left atrial volume index (26 ± 3.5 vs. 30 ± 3.4, P=.001). Left ventricular geometry in the non-dippers also showed increased concentric remodeling, concentric and eccentric hypertrophy.

Conclusions: Our study demonstrates that nocturnal non-dipping of blood pressure in normotensive Blacks of Caribbean origin may be associated with cardiovascular end organ damage thereby providing new surveillance and therapeutic targets. *Ethn Dis*.2016;26(3):279-284; doi:10.18865/ed.26.3.279

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Introduction

Blood pressure fluctuates over a 24-hour sleep/wake cycle; the normal dipping blood pressure profile (DP) has an average night-time blood pressure approximately 15% lower than daytime values.[1] A non-dipping blood pressure profile (NDP) is defined as failure of the nocturnal blood pressure to fall by at least 10% of day-time blood pressure.[1-3] In hypertensive patients, independent of the degree of hypertension, a non-dipping blood pressure pattern is a risk factor for the development of end organ damage, including left ventricular hypertrophy (LVH), congestive heart failure, stroke, carotid media intima thickening and microalbuminuria.[4-9] In patients with normal blood pressure, NDP can also lead to end organ damage as seen on echocardiography, bio-inflammatory markers and microalbuminuria.[10-13] In a prospective study of individuals with normal 24-hr blood pressure, a 5% decrease in the nocturnal decline in diastolic blood pressure was significantly associated with a 20% increase in cardiovascular mortality risk.[14]

Several studies have demonstrated that NDP is more common in Black hypertensives compared with other races.[15-18] Cardiovascular mortality and morbidity is also more pronounced in the Black population,[19-21] with many attributing this disparity mainly to increased risk factors like obesity, diet, poor access to health care and other socioeconomic determinants of health.[22-26] However, there are suggestions that there may be underlying physiological differences

that underpin these effects[27,28] and the pathogenicity of a non-dipping blood pressure profile in the Black population could play a key role in this.[15-17] However, data on cardiovascular target organ effects of NDP in the Black population are sparse. In our study, we aimed to determine if a non-dipping ambulatory blood pressure profile in a cohort of Black patients with normal blood pressure was associated with objective evidence of cardiovascular target organ damage.

Methods

The study was approved by the institutional review board at the Heart Institute of the Caribbean in Kingston, Jamaica. We recruited healthy Black Caribbean normotensive patients in the Kingston area who were aged >18 years. Demographic data, medical history, medications, smoking and alcohol usage history were obtained. Height and weight were measured using a stadiometer, and body mass index (BMI) was calculated as weight (kg)/height (m)^2. Patients were classified as overweight if BMI was 25 kg/m^2 to < 30 kg/m^2, and obese if BMI ≥ 30 kg/m^2.

Office blood pressure (OBP) was measured in both arms with patient sitting using an oscillometric BP device (the GE Dinamap Procure 400 monitor). Three readings were made in each arm and an average was taken. The arm with the higher average was recorded for each study participant. Systolic and diastolic (phase V) BP were determined to the nearest 2 mm Hg. Ambulatory blood pressure (ABP) was measured with the Tonoport V monitor (GE CS V67 [21]) for a minimum of 24 hours, using a similar sized cuff as was used in the OBP measurement. Ambulatory monitors were checked monthly against a mercury manometer and deviation by >4 mm Hg warranted recalibration. The ABP monitor measured BP at 15-minute intervals from 0600 hours to 2200 hours (representing daytime) and 30-minute intervals from 2200 hours to 0600 hours (representing night time). Participants kept a diary card for the duration of the record to note bed time and waking time so as to define day and night to check the transition time. ABP data were interpreted in accordance with British Hypertension Society protocols.[29] ABP data processing was performed using the GE Cardiosoft™ (PAR Medizintechnik GmbH Sachsendammb D-10829, Berlin, Germany) ambulatory blood pressure software.

In our study, we aimed to determine if a non-dipping ambulatory blood pressure profile in a cohort of Black patients with normal blood pressure was associated with objective evidence of cardiovascular target organ damage.

Two-dimensional echocardiogram and Doppler imaging were performed on all study participants by a single echocardiographer (to reduce inter-operator variability) in accordance with American Society of Echocardiography (ASE) protocol, and the following parameters were recorded: relative wall thickness (RWT), left ventricular mass (LVM), left ventricular mass index (LVMI), left atrial volume (LAV) and left atrial volume index (LAVI). Management of data and statistical analysis were performed with EPI Info 3.5.3 (CDC, Atlanta, GA). Proportions were reported as percentages and compared between groups with the Chi-square test.

Results

The mean age of the cohort of the 43 patients was 52 (± 15) years; 67.5% were females. Patients were classified into two groups based on ABP measurements: DP (n=20) and NDP (n=23). There were no statistically significant differences between both groups with respect to age, sex, weight, height, BMI or office blood pressure (OBP). There was a statistically significant difference in sleeping BP between DP and NDP, 112 ± 7/64 ± 2 mm Hg vs 117 ± 3/69 ± 2 mm Hg *(P*=.004) (Table 1).

As can be seen in Table 2, when compared with the DP cohort, the NDP cohort showed evidence of cardiovascular target damage on echocardiography with a significantly increased relative wall thickness (.35 ± .07 cm vs .42 ± .05 cm, *P*=.0001), left ventricular mass index (95 ± 14 vs 105 ± 14 g/m2, *P*=.018) and left atrial volume index (26 ± 3.5 vs. 30 ±

Table 1. Baseline clinical and demographic characteristics of two groups

Parameter	Dippers n=20	Non-dippers n=23	P
Age, yrs	48.0 ± 13.8	53.0 ± 17.8	NS
Sex, M/F %	7/13 (35%/65%)	9/14 (39.1%/60.8%)	NS
DM, %	0	1 (4.3%)	NS
Dyslipidemia, n (%)	1 (5%)	4 (17.4%)	NS
Weight, kg	72.7 ± 10.0	76.8 ± 11.6	NS
Height, cm	169.3 ± 12.0	171.1 ± 9.8	NS
BMI, kg/m^2	25.5 ± 3.9	26.1 ± 4.4	NS
BSA, m^2	1.87 ± .02	1.89 ± 0.03	NS
Heart rate, beats/min	77.4 ± 15.5	78.2 ± 14.3	NS
Office SBP	123.8 ± 12.3	124.1 ± 11.5	NS
Office DBP	73.1 ± 9.3	70.7 ± 7.6	NS
PP, mm Hg	50.7 ± 8.3	53.4 ± 12.2	NS
MAP, mm Hg	89.9 ± 9.6	88.5 ± 7.0	NS
24-hr SBP	122.5 ± 6.7	120.6 ± 5.6	NS
24-hr DBP	76.7 ± 3.6	75.1 ± 4.1	NS

Data are mean ± SD or n(%).
DM, diabetes mellitus; M, male; F, female; BMI, body mass index; BSA, body surface area; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

3.4, *P*=.001). Left ventricular geometry in the non-dippers also showed increased concentric remodeling, concentric and eccentric hypertrophy.

An interesting observation to be made in the results is that, even though the average awake SBP in the DP cohort was significantly higher than the average awake SBP in the NDP cohort, there are more deleterious end organ effects in the NDP cohort and these may be explained by the non-dipping profile.

Table 2: Comparison of echocardiographic findings in dippers vs non-dippers

Parameter	Dippers n=20	Non-dippers n=23	P
Awake SBP	127.4 ± 6.6	117.9 ± 6.9	0
Awake DBP	80.6 ± 4.0	73.9 ± 5.1	0
Sleep SBP	111.9 ± 6.8	116.7 ± 3.2	.004
Sleep DBP	64.2 ± 2.4	68.5 ± 1.7	0
RWT	.35 ± .07	.42 ± .05	.001
LVM	177.0 ± 31.6	199.7 ± 34.3	.031
LVMI	94.5 ± 14.0	105.2 ± 14.4	.018
LAV	48.2 ± 6.6	56.4 ± 7.1	0
LAVI	25.8 ± 3.5	29.9 ± 3.4	.001
NG	18 (90.0%)	13 (56.5%)	.05
CR	1 (5.0%)	3 (13.0%)	-
CH	1 (5.0%)	5 (21.7%)	-
EH	0	2 (8.7%)	-
AG	5 (25.0%)	10 (43.5%)	NS

Data are mean ± SD or n(%).
RWT, relative wall thickness; LVM, left ventricular mass; LVMI, left ventricular mass index; LAV, left atrial volume; LAVI, left atrial volume index; SBP, systolic blood pressure; DBP, diastolic blood pressure; NG, normal geometry; CR, concentric remodeling; CH, concentric hypertrophy; EH, eccentric hypertrophy; AG, abnormal geometry.

Discussion

The pathophysiological mechanism behind a non-dipping profile has not been fully elucidated, but a non-dipping profile is frequently associated with salt-sensitive forms of hypertension, subtle renal injury and mineralocorticoid-induced forms of hypertension.[30] Epidemiologically, salt sensitivity is more common in the Black population and this might explain the racial differences observed in non-dipping blood pressure profiles.[15-18, 30-33] Our cross-sectional study demonstrates that a non-dipping 24 hour ABP profile in normotensive healthy Blacks is associated with evidence of cardiac damage evidenced by the changes in cardiac geometry as described. The higher, sustained blood pressures at night may have had a cumulative effect on cardiac structure over time.

Previous studies in non-Black populations have shown that, in normotensive patients, a non-dipping profile is associated with target organ damage.[10-14] Hoshide et al studied 74 community-dwelling Japanese normotensives and showed that atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and LVMI were increased in non-dippers compared with dippers.[10] An increase in these parameters is established evidence of cardiac remodeling and left ventricular hypertrophy, which sig-

nify early cardiac dysfunction. Soylu et al examined 82 Turkish patients with metabolic syndrome and found evidence of more diastolic cardiac dysfunction in non-dippers compared with dippers.[11] Comparisons between nocturnal hypertension and non-dipping status is sparse in the medical literature.[4,9] Androulakis et al found a stronger association of nocturnal hypertension with subclinical atherosclerosis and cardiac remodeling compared with nocturnal non-dipping status, however the study participants were all hypertensives.[9]

Our study suggests that in Black normotensives, a non-dipping BP pattern was associated with cardiovascular target organ damage, thereby highlighting the importance of establishing dipping status to guide stratification in an intrinsically high-risk population for the consequences of hypertension.

Our study suggests that in Black normotensives, a non-dipping BP pattern was associated with cardiovascular target organ damage, thereby highlighting the importance of establishing dipping status to guide stratification in an intrinsically high-risk population for the consequences of hypertension. The Black race is independently associated with higher levels of target end organ damage in hypertensives;[34,35] thus, targeting non-dipper normotensives may help early targeted therapy and appropriate lifestyle modification.

A few small studies have shown that sodium restriction and use of diuretic antihypertensive medications can shift the circadian rhythm of blood pressure from non-dipper to dipper status in essential hypertension.[36,37] However, whether cardiovascular outcome improves by changing the dipping status pharmacologically remains to be proven.

Study Limitations

Our study is limited by a relatively small sample size and a cross-sectional design. Larger studies are needed in the future to utilize a prospective study design to replicate or confirm these findings, ascertain long-term outcomes in patients with a non-dipping blood pressure status, as well as identify possible risk factors for non-dipping nocturnal blood pressure.

Conclusions

Our study demonstrates that nocturnal non-dipping of blood pressure in normotensive Blacks may be associated with cardiovascular end organ damage. Given the global burden of hypertension and its huge contribution to cardiovascular mortality, this observation may suggest a need for more research into profiling blood pressure dipping status in patients with normal blood pressure. Such future studies may create potential new targets for cardiovascular risk stratification and may afford opportunities to mitigate future hypertension-related end organ damage cardiovascular risk stratification and future hypertension-related end organ damage.

Acknowledgments

Ethical Approval

Our research was approved by the DOCS Heart Center Nigeria institutional review board (IRB) and Heart Institute of the Caribbean IRB and all procedures followed were in accordance with the ethical standards of the IRB and the Helsinki Declaration of 1975, as revised in 2000.

Informed Consent

Written informed consent was obtained from all individuals who participated in the study.

Conflict of Interest

No conflicts of interest to report.

Author Contributions

Research concept and design: Madu E, Baugh D, Mezue; Acquisition of data: Madu E, Baugh D, Madu C; Data analysis and interpretation: Mezue, Isiguzo, Nwuruku; Manuscript draft: Mezue, Madu C, Rangaswami; Statistical expertise: Mezue, Rangaswami; Acquisition of funding: Madu E; Administrative: Madu E; Supervision: Madu E, Baugh, Rangaswami

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