**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\textsuperscript{27,28} and the pathogenicity of a non-dipping blood pressure profile in the Black population could play a key role in this.\textsuperscript{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 $\geq 30$ 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.\textsuperscript{29} ABP data processing was performed using the GE Cardiosoft\textsuperscript{\textregistered} (PAR Medizintechnik GmbH Sachsendamm D-10829, Berlin, Germany) ambulatory blood pressure software.

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 $52 \pm 15$ 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, $112 \pm 7/64 \pm 2$ mm Hg vs $117 \pm 3/69 \pm 2$ mm Hg ($P=0.004$) (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 ($0.35 \pm 0.07$ cm vs $0.42 \pm 0.05$ cm, $P=0.001$), left ventricular mass index ($95 \pm 14$ vs $105 \pm 14$ g/m$^2$, $P=0.018$) and left atrial volume index ($26 \pm 3.5$ vs. $30 \pm$...
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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.

**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 LVM 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-

### Table 1. Baseline clinical and demographic characteristics of two groups

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

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.

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

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

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 index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.
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.\textsuperscript{11} Comparisons between nocturnal hypertension and non-dipping status is sparse in the medical literature.\textsuperscript{4,9} Androulakis et al found a stronger association of vascular 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;\textsuperscript{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.\textsuperscript{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 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, Nwuru; Manuscript draft: Mezue, Madu C, Rangaswami; Statistical expertise: Mezue, Rangaswami; Acquisition of funding: Madu E; Administrative: Madu E; Supervision: Madu E, Baugh, Rangaswami

References
8. Ingelsson E, Björklund-Bodegård K, Lind
3. Staessen JA, Bieniaszewski L, O'Brien
20. Jolly S, Vittinghoff E, Chattopadhyay A, Thijs
16. Gretler DD, Fumo MT, Nelson KS, Murphy
differences in the hypertensive heart and 24-hour blood pressure profile. Hyper-
doi.org/10.1161/01.HYP.31.5.1190.
prognostic significance of the nocturnal de-
cline in blood pressure in individuals with and
without high 24-h blood pressure: the Ohasa-
ma study. J Hypertens. 2002;20(11):2183-
2189. http://doi.org/10.1097/00004872-
20021100000017. PMID:12409596.
JR. Blunted sleep-time relative blood pressure
decline increases cardiovascular risk indepen-
dent of blood pressure level—the “normoten-
sive non-dipper” paradox. Chronobiol Int.
12. Myredal A, Friberg P, Johansson M. Elevated
cardiovascular risk associated with blunted
nighttime relative blood pressure decline:
the Ohasama study. Turk Kardiyol Dern Arz.
11. Soylu A, Güleç H, Alhanoğlu YI, Sümmez O,
Ayhan SS, Gök H. The effect of nondipper
blood pressure pattern on target organ damage
in patients with metabolic syndrome. Turk
10. PMID:20098038.
myocardial repolarization liability and arterial
baroreflex dysfunction in healthy individuals
with nondipping blood pressure pattern. Am J
doi.org/10.1038/ajh.2009.252. PMID:20075850.
JR. Blunted sleep-time relative blood pressure
decline increases cardiovascular risk indepen-
dent of blood pressure level—the “normoten-
sive non-dipper” paradox. Chronobiol Int.
7. Metoki H, Ohkubo T, Kikuya M, et al. Prog-
nostic significance for stroke of a morning
pressor surge and a nocturnal blood pressure
decline: the Osaka study. Hypertension.
doi.org/10.1161/01.HYP.0000198541.12640.0F.
PMID:16380533.
6. Ingelsson E, Bjorklund-Bodegard K, Lind
L, Arnlöv J, Sundström J. Diurnal blood
pressure pattern and risk of congestive heart
PMID:16804152.
5. Androulakis E, Papageorgiou I, Chatzistam-
tiou E, Kallikazaros I, Stefanadis C, Toussoulis
D. Improving the detection of preclinical or-
gan damage in newly diagnosed hypertension:
nighttime hypertension versus non-dipping
pattern. J Hum Hypertens. 2003;17(9):509-
PMID:12979900.
Database on Ambulatory Blood Pressure In
Relation to Cardiovascular Outcomes Investi-
gators. Prognostic value of isolated nocturnal
hypertension on ambulatory measurement in
8711 individuals from 10 populations. J
doi.org/10.1097/01.HYP.000037833b49fe.
PMID:20520575.
3. Tsivgoulis G, Vemmos KN, Zakopoulos N,
et al. Association of blunted noct-
urnal blood pressure dip with intrace-
1097/01.mp.0000172706.51792.0f.
PMID:16077264.
Assocations between nondipping of nocturnal
blood pressure decrease and cardiovascular
target organ damage in strictly selected
community-dwelling normotensives. Am J
doi.org/10.1016/S0895-7061(03)00567-3.
PMID:12799090.
1. Soylu A, Güleç H, Alhanoğlu YI, Sümmez O,
Ayhan SS, Gök H. The effect of nondipper
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