The Association of Blunted Nocturnal Blood Pressure Dip and Stroke in a Multiethnic Population

Robert A. Phillips, Kara F. Sheinart, James H. Godbold, Rashid Mahboob, and Stanley Tuhrim

Nondipping has been defined as a reduction in the mean systolic and diastolic blood pressure (BP) of <10% from awake to sleep. We hypothesized that nondipping might be associated with stroke in minority populations. We monitored BP over a 24-hour period with an ambulatory device in 166 cases from a multiethnic population of stroke survivors (63 blacks, 61 non-Hispanic whites, and 42 Caribbean Hispanics, aged 69.5 ± 11 years) and 217 community control subjects (73 blacks, 107 non-Hispanic whites, and 67 Caribbean Hispanics, aged 69 ± 9 years). Prevalence of nondipping was significantly greater among cases than among control subjects (64% vs 37%, P < .001). In a multiple logistic regression model adjusted for traditional risk factors for stroke, nondipping conferred an increased risk for stroke. Probability of stroke associated with nondipping (odds ratio [OR] 2.5, confidence interval [CI] 1.6 to 4.0) was equal to that of traditional risk factors. Nondipping increased the chance of having a stroke in both non-Hispanic whites (OR 4.2, P < .001) and blacks/Caribbean Hispanics (OR 1.9, P = .03). The strength of the contribution of nondipping to stroke risk was similar in all ethnic groups. Nondipping was associated with stroke in both men and women. Given the previous reports that nondipping contributes to stroke risk in European and Asian populations, these data suggest that nondipping may be universally associated with risk for stroke. Am J Hypertens 2000;13:1250–1255 © 2000 American Journal of Hypertension, Ltd.

KEY WORDS: Stroke, ambulatory blood pressure monitoring, essential hypertension, nocturnal blood pressure, race.

Higher blood pressure (BP) while awake and lower BP (a “dip”) while asleep characterizes BP in most normotensive and hypertensive individuals. Patients can therefore be classified into dippers and nondippers via 24-hour ambulatory BP monitoring (ABPM). Nondippers have been defined as having a reduction in the mean systolic and diastolic BP of <10% from awake to sleep. In some studies the absence of this nocturnal decline has been associated with increased risk for heart disease and stroke. Compared to non-Hispanic whites, individuals of Caribbean Hispanic descent living in New York City have an increased mortality and morbidity from...
stroke. Blacks also have an increased incidence of stroke. Some studies, but not all, suggest that there may be racial/ethnic differences in 24 h BP profiles, and that blacks are more likely to be nondippers. However, the association between stroke risk and nondipping in blacks and Caribbean Hispanics has not been studied. We attempted to assess this in the Minorities, Risk Factors and Stroke Study (MRFASS), a case-control study in a multiethnic population in New York City.

**METHODS**

**Patient Selection and Controls** The Minorities, Risk Factors and Stroke Study (MRFASS) evaluated the impact of certain stroke risk factors in a multiethnic population that includes non-Hispanic whites, blacks, and Caribbean Hispanics. The latter two groups are traditionally characterized as minorities in the United States. Details of the methodology and baseline characteristics of the population have been published previously. Our study population consisted of 166 cases of stroke (excluding subarachnoid hemorrhage) and 217 community control subjects. Patients and control subjects were recruited predominantly from the catchment area of the Mount Sinai Hospital, which includes East and Central Harlem as well as the Upper East and West Sides of Manhattan in New York City. Stroke subtype was categorized as follows: large vessel atherothrombotic, cardioembolic, lacunar, infarct of unknown cause, intracerebral hemorrhage, infarct of multiple etiologies, and infarct of unusual etiology. Level of physical activity poststroke was quantified with the Barthel score.

**Ambulatory BP Monitoring** From 1 week to 4 years poststroke, 24 h ABPM was performed as previously described, with the following differences: 1) BP was measured every 20 min during awake hours and every 30 min during sleep; and 2) the SpaceLabs 90217 device (SpaceLabs, Redmond, WA) was used in this study. Awake and sleep periods were determined by diary entries. Dipping was defined as a decrease in sleep BP of $10\%$ in either systolic or diastolic BP. Nondipping was defined as a $10\%$ decrease in both sleep systolic and diastolic BP compared with awake BP. The ABPM was performed in the same manner in control subjects. Hypertension, on the basis of ambulatory BP monitoring, was defined as a daytime systolic BP of $\geq 135$ mm Hg.

**Statistical Methods** Differences in demographic characteristics between patients and control subjects were tested with the Student $t$ test or by the $\chi^2$ test. Multiple logistic regression models for stroke risk associated with nondipper status were developed, adjusting for known risk factors for stroke (SAS version 6.12, SAS Institute, Cary, NC).

**RESULTS**

**Patient Characteristics** The age for the patients was typical of that for first stroke occurrence, and there was no significant difference between patients and control subjects. There were more women among the control subjects but body mass index (BMI) and the ethnic distribution was similar. As expected, risk factors for cardiovascular disease were more prevalent among patients. Blood pressure was higher...
and decreased significantly less during sleep in patients than in control subjects. This was a heterogeneous group of stroke patients with the following stroke subtype breakdown: large vessel atherothrombotic (n = 16), cardioembolic (n = 29), lacunar (n = 58), infarct unknown cause (n = 28), intracerebral hemorrhage (n = 20), infarct of multiple etiologies (n = 10), and infarct of unusual etiology (n = 2). There were only two patients whose lesions included the insular cortex.

Prevalence of Nondipping Status  Nondipping status was 1.7-fold more prevalent among patients than control subjects (Table 1). When unadjusted for traditional stroke risk factors, both black and non-Hispanic white patients had significantly higher prevalence of nondipping compared with control subjects, whereas this difference was of borderline significance in Caribbean Hispanics (Table 2). There was a higher prevalence of nondipping among Caribbean Hispanic control subjects compared with non-Hispanic whites and blacks. There was a trend toward a greater prevalence of nondippers among Hispanic patients compared with control subjects. In controls, there was no apparent effect of age on prevalence of nondipping, but among patients there was a significant increase in nondipping with age (Table 3).

Association of Nondipping Status and Stroke  For the group as a whole, nondipping status was significantly associated with stroke in a logistic regression model that adjusted for systolic and diastolic ambulatory (waking or 24 h) blood pressure, age, gender, race, history of hypertension, hypertensive medications, current smoking, history of diabetes, and BMI (Table 4, Fig. 1). When evaluated separately, nondipping status was significantly associated with stroke in both the non-Hispanic white population (OR = 4.2, P < .001) and the minority populations (blacks/Caribbean Hispanics, OR = 1.9, P = .03). These OR did not differ significantly from each other (z = 1.5, P = NS).

Time interval between stroke and ABPM was not related to nondipping status—there was no statistically significant difference in the frequency of nondipping between subjects who had ABPM within 6 months from stroke and those who had ABPM performed > 6 months poststroke. Level of activity poststroke also was not significantly associated with nondipping status.

History of hypertension, current smoking, and history of diabetes were also significant risk factors for stroke, but BMI was not. The OR associated with nondipping (OR = 2.5, CI 1.6 to 4.0, P < .001) was comparable to the OR for these traditional risk factors. The adjusted OR for stroke associated with nondipping was significant in women (OR = 1.9, CI 1.02 to 3.4, P < .05), and in men (OR = 4.3, CI 1.9 to 9.6, P < .001).

TABLE 2. DIPPER STATUS FREQUENCIES BY RACE/ETHNIC GROUP, UNADJUSTED FOR TRADITIONAL RISK FACTORS

<table>
<thead>
<tr>
<th></th>
<th>Dippers</th>
<th>Nondippers</th>
<th>% Nondippers</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blacks Patients</td>
<td>25</td>
<td>38</td>
<td>60.3</td>
<td>&lt;.01*</td>
</tr>
<tr>
<td>Control subjects</td>
<td>46</td>
<td>27</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic whites Patients</td>
<td>22</td>
<td>39</td>
<td>63.9</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Control subjects</td>
<td>67</td>
<td>30</td>
<td>30.9</td>
<td></td>
</tr>
<tr>
<td>Caribbean Hispanics Patients</td>
<td>13</td>
<td>29</td>
<td>69.1</td>
<td></td>
</tr>
<tr>
<td>Control subjects</td>
<td>23</td>
<td>24</td>
<td>51.1†</td>
<td>.08*</td>
</tr>
<tr>
<td>Total Patients</td>
<td>60</td>
<td>106</td>
<td>63.9</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Control subjects</td>
<td>136</td>
<td>81</td>
<td>37.3</td>
<td></td>
</tr>
</tbody>
</table>

* P value for difference in % nondippers between patients versus control subjects.
† P = .03 for difference in % nondippers between blacks/non-Hispanic whites versus Caribbean Hispanic control subjects.

TABLE 3. PERCENT DIPPER STATUS BY AGE

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Patients</th>
<th>Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>44.1%</td>
<td>37.5%</td>
</tr>
<tr>
<td>60–69</td>
<td>61.9%</td>
<td>37.7%</td>
</tr>
<tr>
<td>≥70</td>
<td>72.2%*</td>
<td>37.0%†</td>
</tr>
</tbody>
</table>

* P = .01 within patients.
† P = 1.0 within control subjects.
DISCUSSION

In this case-control study of a multiethnic population, we found that nondipping status was associated with an increased probability of having a stroke even after adjustment for traditional stroke risk factors. This risk was seen in non-Hispanic whites as well as in the minority populations. The association of nondipping with stroke is equal in magnitude to that of traditional risk factors for stroke, and is similar in women and men.

To our knowledge, this is the first report demonstrating that nondipping is associated with stroke risk in a case-control study of a multiethnic population that includes blacks and Caribbean Hispanics. Our data suggest that nondipping with stroke is equal in magnitude to that of traditional risk factors for stroke, and is similar in women and men.

To our knowledge, this is the first report demonstrating that nondipping is associated with stroke risk in a case-control study of a multiethnic population that includes blacks and Caribbean Hispanics. Our data suggest that nondipping is a risk factor for stroke that appears to be of similar magnitude in all ethnic groups. In addition, we found that nondipping was associated with age in stroke survivors but not in control subjects. Thus, nondipping seems to be a more powerful risk factor for stroke in an elderly population than in younger subjects.

Several studies in a variety of populations of European and Asian descent have demonstrated a relationship between nondipping and risk for cardiovascular events, including stroke. In a case-control study of 123 patients, O’Brien et al\(^1\) found that nondippers (< 10/5 mm Hg decrease in systolic and diastolic BP) had a significantly higher frequency of stroke than dippers (23.8% vs 2.9%, \(P < .001\)). In a large prospective trial of 1187 Italian subjects (aged 45 ± 15 years) followed for up to 7.5 years, Verdecchia et al\(^3\) found that nondippers had a significantly greater risk for cardiovascular events than did dippers. This difference persisted even after adjustment for 24 h systolic and diastolic BP values, suggesting that it was the pattern of the BP, not simply the level of BP, that affected outcome. We confirm these results by finding that adjustment for the current level of BP did not alter the risk for stroke associated with nondipping. In the study by Verdecchia et al, there was a gender difference in the effect of nondipping on outcome. In women, the presence of nondipping conferred nearly a sevenfold increased relative risk for cardiovascular morbid events, but in men the relative risk was unaltered by nondipping. By contrast, our data suggest that nondipping is associated with stroke risk in both men and women.

In a case-control study of patients with acute lacunar infarcts, those with blunted fall in nocturnal BP had the greatest odds ratio for stroke.\(^5\) A prospective study on the outcomes of patients with symptomatic

### TABLE 4. LOGISTIC REGRESSION MODEL FOR STROKE RISK, ADJUSTED FOR BLOOD PRESSURE, AGE, GENDER, RACE, BODY MASS INDEX, AND ANTIHYPERTENSIVE MEDICATIONS

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondipper</td>
<td>2.5</td>
<td>1.6–4.0</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>2.6</td>
<td>1.6–4.3</td>
</tr>
<tr>
<td>Current smoking</td>
<td>3.2</td>
<td>1.7–6.4</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>3.0</td>
<td>1.6–4.0</td>
</tr>
</tbody>
</table>

*OR = odds ratio; CI = confidence interval.*

![FIG. 1. Adjusted odds ratios with 95% confidence intervals for risk for stroke associated with nondipping status within the groups studied. Minorities are the combined subjects of black and Caribbean Hispanic descents. Odds ratio derived from a logistic regression model that adjusted for age, history of hypertension, history of diabetes, current smoking, gender, and body mass index. In the “overall” model, the logistic regression also adjusted for ethnicity/race. The odds ratios for the non-Hispanic whites versus the minorities were not significantly different from each other.](https://academic.oup.com/ajh/article-abstract/13/12/1250/226823)
lacunar infarcts measured 24-h BP 4 weeks after the stroke and then after an average follow-up of 3.2 years. Those who sustained new cerebrovascular events had a significantly smaller drop in nocturnal BP at baseline and at follow-up compared with those who developed no new lesions or remained asymptomatic. In a study of healthy elderly normotensive men and women, higher nocturnal BP and blunted fall in nocturnal BP were associated with subcortical lesions detected on MRI. Finally, there is a report that extreme dipping, characterized by a > 20% drop in nocturnal systolic BP, is associated with an increased stroke rate. Because of the small number of extreme dippers in our sample, we were unable to assess the association of this phenomenon with stroke.

Although prospective and observational data suggest that nondipping may contribute to risk for stroke, it is also very likely that, in some patients, abnormalities of sleep BP are either exacerbated or caused by the stroke. For example, patients with acute thromboembolic hemispheric strokes that involve the insular cortex, a region involved in autonomic regulation, have a tendency toward a rise in nocturnal BP, whereas those patients with hemispheric strokes that spare the insular cortex tend to have only a blunted fall in nocturnal BP. Similarly, acute subcortical infarcts do not appear to affect diurnal BP variation, whereas cortical infarcts and primary intracerebral hemorrhages significantly blunt nocturnal decline in BP. In addition, the lower level of diurnal activity in stroke survivors can theoretically reduce day–night BP differences. This is a less likely possibility in our study, as we did not find a statistically significant difference in the frequency of dipping between subjects who were able to walk and those confined to a wheelchair. Thus, a conservative interpretation of our data is that nondipping is associated with stroke but may not be causative; case-control design cannot determine causality. More prospective data are needed to determine the role that nondipping contributes to causation of stroke and to recurrent stroke rate.

ACKNOWLEDGMENTS

The authors thank Alexander Butkevich, MD, MSc for reading the manuscript and for very helpful comments. This work was supported by NIH grants 2-RO1-NS29762, 1K08-NS01869, and by NIH grant 5-MO1-RR-00071 to the General Clinical Research Center.

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