

## Absence of Nocturnal Dipping is Associated with Stroke and Myocardium Infarction

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### Abstract

**Background:** The arterial hypertension varies in according to the circadian cycle, presenting physiologic fall of blood pressure (BP) during sleep (dipping). The absence of this fall or its increase associates to higher incidence of target-organ damages.

**Objective:** To analyze the prevalence of dipping in hypertensive individuals, to correlate dipping to the blood pressure levels, clinic, and socio-demographic factors, and biochemical characteristics and to associate it cardiovascular events (stroke and myocardial infarction).

**Methods:** Hypertensive individuals were submitted to the ambulatory blood pressure monitoring. Presence of dipper was defined as fall  $\geq 10\%$  of the systolic BP of the day for sleep.

**Results:** 163 evaluated patients were divided in dippers (D, n=53) and nondippers (ND, n=110). Between the groups there was not significant difference to the age, sex, race, time of hypertension, glycemia, LDL-cholesterol, total cholesterol, triglycerides, schooling, smoking, and history of diabetes. D presented BP higher than the ND during the day and lower during sleep. ND had higher body mass index (BMI) ( $p=0.0377$ ), lower level of HDL-cholesterol ( $p=0.0189$ ), and higher pulse pressure during sleep ( $p=0.0025$ ). History of stroke alone ( $p=0,046$ ) and combined with myocardial infarction ( $p=0.032$ ) were more frequent in nondippers individuals. In the logistic regression, only ND was associated independently with stroke or myocardial infarction.

**Conclusion:** ND was associated in an independent way with the target-organ damages analyzed, what demonstrates its importance and strengthens the necessity of more aggressive treatment with objective to reach BP goals e, consequently, to prevent the development of new cardiologic and cerebrovascular events. (Arq Bras Cardiol 2010; 94(1) : 74-80)

**Key Words:** blood pressure monitoring, ambulatory; hypertension; stroke; myocardial infarction.

### Introduction

Blood pressure (BP) varies according to the interaction between neural-humoral, behavioral and environmental factors. One of the complementary exams capable of assessing this pressure pattern in a 24-hour period is the ambulatory blood pressure monitoring (ABPM), which allows the indirect and intermittent register of BP, thus enabling the understanding of its variation profile at vigil and sleep periods. According to the Brazilian guidelines on ABPM, systemic arterial hypertension (SAH) is characterized by values superior to 130/80 mmHg<sup>1</sup> during 24-hour period. Nowadays, there is evidence that the values obtained by ABPM prognosticate better the most significant cardiovascular events, such as myocardium infarction and stroke, in comparison to the values found in consultation rooms<sup>2-6</sup>.

Among the parameters assessed by ABPM, some deserve to be emphasized. In analysis of the Syst-Eur study<sup>6</sup>, the variable which showed better correlation to the main cardiovascular events was systolic blood pressure during sleep, followed by 24-hour and vigil systolic blood pressure. Another variable that deserves to be emphasized is the pressure drop which occurs in the vigil to sleep period, called nocturnal dipping (ND). With regard to the prognostic bound to this variable, whose normality value is a minimum 10% reduction of BP during sleep period in relation to vigil, it is known that there is an inverse correlation of BP during sleep and cardiovascular outcomes, even in the presence of normal mean values of pressure obtained by ABPM<sup>4</sup>.

On account of the importance bounded to the gauging of 24-hour pressure levels and the worse cardiovascular prognosis represented by the individual without ND, this study had the following objectives: to assess the prevalence of ND among individuals with SAH, to correlate ND to pressure levels, clinical variables, sociodemographic and biochemical factors and to associate them with cardiovascular events (stroke and myocardium infarction).

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## Methods

A group of 163 hypertensive individuals, followed-up in a specialty ambulatory, were assessed and, later on, divided into groups with and without nocturnal dipping (dipper and non-dipper). The patients presented SAH diagnosis for at least three years. All participants signed the informed consent, which was previously approved by the Ethics Committee of the institution.

For the assessment of comorbidities, data regarding the presence of diabetes mellitus (DM), history of stroke, dislipidemia (DLP), medicines in usage, body mass index [IMC = kg/height (m<sup>2</sup>)], school degree, sex and other risk factors or necessary information obtained from the medical record were investigated.

The patients who already presented diagnosis were considered diabetic individuals due to the presence of at least two fast glycemia dosages  $\geq 126$  mg/dL or to altered glucose oral tolerance test (OGTT)<sup>7</sup>. Patients who had OGTT in the range of glucose intolerance, that is, glycemia of two hours after taking dextrosol with values between 140 and 199 mg/dL, were studied in the non-diabetic group, even when under treatment with metformin (three patients), which is recommended for such cases<sup>8</sup>. Analysis of stroke episodes was carried out based on clinical history, presence of sequel and events previously identified in the medical record. MI diagnosis was based on clinical history and confirmed by analysis of medical records that showed previous enzymatic alterations (troponin and CK-MB), electrocardiographic alterations suggestive of coronary ischemia and proper treatment for this situation.

DLP was identified by total cholesterol dosages (TC), high-density lipoprotein cholesterol fraction (HDL-c) and triglycerides (TG) after 12-hour fasting<sup>9</sup>. The following reference values were adopted: TC < 200 mg/dL, HDL-c > 40 mg/dL, low-density lipoprotein cholesterol fraction (LDL-c) < 130 mg/dL and TG < 150 mg/dL. LDL-c fraction was calculated by means of the formula: LDL-c = TC - HDL-c - TG/5 (for TG < 400 mg/dL)<sup>10</sup>. Individuals with alterations in the aforementioned parameters and/or those who were under treatment with HMG-CoA reductase inhibitors or other hypolipemic medicines were considered as patients with dislipidemia.

The values of systolic (SBP) and diastolic blood pressure (DBP) were obtained from 24-hour ABPM, as mean values obtained in 24 hours (\_m), vigil (\_v) and sleep (\_s) periods were considered in the analysis. Pulse pressure (PP) was calculated with the mean values of SBP and DBP during the assessed periods (24 hours, vigil and sleep) in the formula PP = SBP - DBP. ND was standardized as drop  $\geq 10\%$  of SBP in the period of vigil to sleep. The values of  $\leq 130/80$  within 24 hours,  $\leq 135/85$  during vigil and  $\leq 120/70$  mmHg during sleep were considered normal<sup>1</sup>.

Spacelabs 90207 with its software for equipment programming and written reports emission was used. The installation of the equipment was made during the day, and the patient remained with it for a 24-hour period. The process of monitoring was carried out in dais that represented the patients' daily activities. The equipment was programmed to register BP measurements every 15 minutes during vigil and every 20 minutes during sleep. All participants were instructed

as part of the exam protocol and registered their daily activities, meal, waking up and sleeping timetables, besides medications horary and presence of symptoms. Therefore, the definitions of vigil and sleep periods were based on the patients' timetables.

The calculated size of the sample, admitting  $\alpha$  deviation of 1% as to reject the hypothesis of nullity, was 47. For the comparison between groups, the software GraphPad Instat 3.0 was used, and the Fisher's Exact test and Mann-Whitney test were applied for categorical and continuum variables, respectively. The multivariate logistic regression model was applied as to identify variables from the multivariate analysis that were statistically significant between groups (BMI, HDL-c and PP\_s) and significantly associated with the studied cardiovascular events. The deviation of  $\alpha$  at 5% with level of significance of  $p < 0.05$  was adopted.

## Results

The general profile of the studied population may be observed on Table 1. The sample was composed by individuals with longtime-diagnosed SAH, whose values of BMI, waist circumference, fast glycemia and mean 24-hour BP were superior to the established limit values.

The studied casuistry consisted of 163 individuals with mean age of  $60.6 \pm 11.6$  years old and time of SAH diagnosis of  $15.8 \pm 10.8$  years. After ABPM analysis, the studied individuals were divided in Dipper (n=53, patients with

**Table 1 - Basal profile of the studied population**

Variable	Mean $\pm$ SD
Age (years old)	60.6 $\pm$ 11.6
SAH time (years)	15.8 $\pm$ 10.8
BMI (Kg/m <sup>2</sup> )	30.3 $\pm$ 5.6
School degree (years of study)	4.0 $\pm$ 3.2
Waist circumference (cm)	107.0 $\pm$ 14.2
SBP_m (mmHg)	134.9 $\pm$ 18.9
DBP_m (mmHg)	80.2 $\pm$ 11.0
SBP_v (mmHg)	138.0 $\pm$ 17.0
DBP_v (mmHg)	82.6 $\pm$ 11.4
SBP_s (mmHg)	129.0 $\pm$ 17.4
DBP_s (mmHg)	73.3 $\pm$ 10.7
Fast glycemia (mg/dL)	117.1 $\pm$ 53.0
HDL-c (mg/dL)	54.4 $\pm$ 14.7
LDL-c (mg/dL)	110.2 $\pm$ 32.5
Triglycerides (mg/dL)	136.6 $\pm$ 73.0
Total cholesterol (mg/dL)	191.3 $\pm$ 40.2
Number of anti-hypertensive medications	2.7 $\pm$ 0.9
SBP dipping (%)	6.4 $\pm$ 7.4

BMI - body mass index; SB - systolic blood pressure; DBP - diastolic blood pressure; \_m - mean 24-hour pressure value; \_v - pressure value during vigil; \_s - pressure value during sleep.

SAH and present ND) and Non-dipper (n=110, hypertensive individuals without ND). Dipper Group was composed of 29 women and 24 men, while Non-dipper Group comprised 62 women and 48 men. Groups did not differ ( $p>0.05$ ) with regard to individuals' mean age, SAH time, school degree and waist circumference (Table 2). With regard to BMI, ND individuals presented lower mean values in comparison to hypertensive patients without ND ( $29.2 \pm 5.0 \times 30.9 \pm 5.7$ ,  $p=0.0377$ ).

Based on ABPM, it was observed that Dipper Group presented pressure levels higher than those of Non-dipper Groups during vigil period for SBP ( $141.6 \pm 16.4 \times 136.2 \pm 17.0$ ,  $p=0.0232$ ) and for DBP ( $86.5 \pm 10.4 \times 80.6 \pm 11.5$ ,  $p=0.0003$ ). During sleep period, Dipper Groups presented mean values lower than those of Non-dipper Group for SBP ( $122.1 \pm 14.1 \times 132.4 \pm 17.9$ ,  $p=0.0001$ ) and DBP ( $70.2 \pm 8.6 \times 74.8 \pm 11.3$ ,  $p=0.0113$ ). Though pressure levels during 24-hour period followed a tendency of higher mean values in Dipper Group, they presented significant differences only for DBP ( $82.5 \pm 9.4 \times 79.0 \pm 11.5$ ,  $p=0.0065$ ), while values for

SBP were not significant ( $p>0.05$ ). When PP of both groups was analyzed, we observed that the individuals from Dipper Group presented lower PP during sleep ( $51.9 \pm 10.9 \times 57.6 \pm 13.5$ ,  $p=0.0025$ ) in comparison to Non-dipper Group. Such relation was not observed for PP during vigil and within the 24-hour period.

Mean HDL-c was higher in patients with ND in comparison to the mean of individuals without it ( $57.4 \pm 14.2 \times 52.9 \pm 14.8$ ,  $p=0.0189$ ). Mean glycemia, TC, LDL-c and TG did not present statistically significant differences between groups.

After analyzing qualitative variables (Table 3), we verified that groups did not differ ( $p>0.05$ ) with regard to sex, skin color, smoking (5.6 versus 6.4%), sedentarism (58.5 versus 50.0%), MI history (1.9 versus 5.8%) in Dipper and Non-dipper Groups, respectively. Though DM and DLP histories have not presented significant p-value, both conditions were more frequent in ND individuals. Groups did not differ either regarding the main anti-hypertensive medications (diuretic, angiotensin-converting enzyme inhibitor, AT1 angiotensin II receptor blocker, calcium channel blockers and beta blockers). Stroke history (RR=1.16 95%CI 1.00-1.33), statin usage (RR=1.36 95%CI 1.07-1.72), hypoglycemic (RR=1.27 95%CI 1.01-1.59) and associate lesions in target-organs (MI or stroke) (RR=1.19 95%CI 1.02-1.39) were related to ND absence.

As groups differed in some clinical characteristics, the logistic regression analysis was carried out as we used the presence of lesions in target-organs as dependent variable (stroke and MI) and as independent variables all clinical variables, including nocturnal dipping. BMI, HDL-c and PP\_s did not constitute factors associated with stroke and MI risk. Only absence of nocturnal dipping presented independent correlation to the presence of assessed lesions in target-organs (Table 4).

**Table 2 – Comparison between continuum variables of groups with and without ND by Mann-Whitney test**

Variable	Dipper (n=53)	Non-dipper (n=110)	p-value
Age (years old)	60.4 ± 12.4	60.6 ± 11.3	NS
SAH time (years)	15.1 ± 12.1	16.1 ± 10.1	NS
BMI (Kg/m <sup>2</sup> )	29.2 ± 5.0	30.9 ± 5.7	0.0377
School degree (years of study)	3.7 ± 3.0	4.2 ± 3.4	NS
Waist circumference (cm)	106.9 ± 11.2	107.1 ± 15.5	NS
SBP_m (mmHg)	134.1 ± 22.6	135.4 ± 16.9	NS
DBP_m (mmHg)	82.5 ± 9.4	79.0 ± 11.5	0.0065
PP_m (mmHg)	54.2 ± 13.3	56.3 ± 12.5	NS
SBP_v (mmHg)	141.6 ± 16.4	136.2 ± 17.0	0.0232
DBP_v (mmHg)	86.5 ± 10.4	80.6 ± 11.5	0.0003
PP_v (mmHg)	55.3 ± 11.6	55.6 ± 12.4	NS
SBP_s (mmHg)	122.1 ± 14.1	132.4 ± 17.9	<0.0001
DBP_s (mmHg)	70.2 ± 8.6	74.8 ± 11.3	0.0113
PP_s (mmHg)	51.9 ± 10.9	57.6 ± 13.5	0.0025
Fast glycemia (mg/dL)	106.3 ± 32.1	122.4 ± 60.0	NS
HDL-c (mg/dL)	57.4 ± 14.2	52.9 ± 14.8	0.0189
LDL-c (mg/dL)	111.7 ± 29.1	109.4 ± 34.1	NS
Triglycerides (mg/dL)	130.9 ± 62.6	139.5 ± 77.7	NS
Total cholesterol (mg/dL)	195.3 ± 37.2	189.4 ± 41.7	NS
Number of anti-hypertensive medications	2.6 ± 0.9	2.7 ± 0.9	NS

BMI - body mass index; SBP - systolic blood pressure; DBP - diastolic blood pressure; PP - pulse pressure; \_m - mean 24-hour pressure value; \_v - pressure value during vigil; \_s - pressure value during sleep; NS - Non-significant ( $p>0.05$ ).

## Discussion

In the present study, there was a high prevalence of attenuation or absence of nocturnal dipping (67.5%). ND attenuation was associated with the presence of other cardiovascular risk factors (obesity and lower HDL-c) and also with a higher frequency of lesion in target-organ. Studies on the prevalence of cardiovascular and cerebral events varies greatly in the specific literature (Table 5), reaching a frequency of 37.5 to 64.2%<sup>11-21</sup> under several factors' influence, like the definition of sleep and vigil periods<sup>22</sup>.

In our sample, ND individuals presented mean pressure superior to those presented by individuals without ND during vigil and inferior during sleep. However, when the 24-hour period was assessed, this behavior pattern was not observed. These findings, in general, differ from those found in literature<sup>14-16,18,19</sup>.

Torun et al<sup>14</sup>, after analyzing hypertensive patients with similar pressure levels during ambulatorial gauging and that never received treatment, observed that patients without ND presented higher mean systolic and diastolic pressures within 24 hours, higher SBP values in vigil and higher SBP and DBP values during sleep in comparison to patients with ND. The authors associated these findings with the high prevalence of lesions in target-organs in the mentioned group, a result which

**Table 3 - Comparison between qualitative variables of groups with and without ND by Fisher's exact test**

Variable	Presence of ND (n=53)	Absence of ND (n=110)	OR	95%CI	p-value
Females - n° (%)	29 (54.7)	62 (56.3)	1.038	0.72-1.49	NS
Smoking - n° (%)	3 (5.6)	7 (6.4)	1.008	0.92-1.09	NS
White skin - n° (%)	29 (54.7)	62 (56.3)	1.014	0.69-1.47	NS
Sedentarism - n° (%)	31 (58.5)	55 (50.0)	0.837	0.57-1.21	NS
DM history - n° (%)	15 (28.3)	42 (38.2)	1.16	0.92-1.45	NS
Stroke history - n° (%)	6 (11.3)	26 (23.6)	1.16	1.00-1.33	0.046
MI history - n° (%)	1 (1.9)	6 (5.8)	1.03	0.97-1.10	NS
DLP history - n° (%)	22 (26.4)	59 (54.1)	1.27	0.94-1.73	NS
Statin usage - n° (%)	14 (26.4)	50 (45.9)	1.36	1.07-1.72	0.013
Usage of hypoglycemic medications - n° (%)	14 (26.4)	46 (42.2)	1.27	1.01-1.59	0.036
Usage of diuretic medications - n° (%)	45 (84.9)	94 (86.2)	1.11	0.44-2.82	NS
Usage of ACEI or ARB - n° (%)	45 (84.9)	90 (82.6)	0.842	0.34-2.07	NS
Usage of CCB - n° (%)	28 (52.3)	56 (51.4)	0.943	0.49-1.82	NS
Usage of beta blockers - n° (%)	14 (26.4)	38 (34.9)	1.49	0.72-3.08	NS
MI or stroke history - n° (%)	7 (13.2)	30 (27.3)	1.19	1.02-1.39	0.032

DM - diabetes mellitus; MI - myocardium infarction; DLP - dislipidemia; ACEI - angiotensin-converting enzyme inhibitors; ARB - AT1 angiotensin II receptor blockers; CCB - calcium channel blockers; RR - relative risk; CI - confidence interval; NS - Non-significant ( $p > 0.05$ ).

is similar to those observed by Anan et al<sup>12</sup>, who emphasized the importance of the method chosen for the investigation of hypertensive patients.

PP seems to be an independent marker of cardiovascular mortality, mainly among individuals older than 50 years old and with history of myocardium infarction, cardiac insufficiency and stroke<sup>23</sup>. The arterial rigidity and the reflection of pulse wave are the greatest determinant factors for PP elevation due to aging. An increase in the arterial rigidity may also elevate the risk for coronary events due to rapid return of pulse wave reflected at the end of systole and the risk for cerebrovascular events due to a modification in the arteries' walls and development of atherosclerotic plaques<sup>24</sup>. In our sample, composed by individuals with mean age superior to 60 years old, we observed higher statistically significant PP in Non-dipper Group during sleep (57.6 mmHg), but no statistical significance in the other periods. According to the IV Brazilian directive for ABPM, the value of 53 mmHg is praised for PP as a limit which is superior to normality<sup>1</sup>. This value was initially showed by Verdecchia et al<sup>25</sup>, who found a higher risk for cardiovascular events when PP was superior to 53 mmHg after evaluating more than 2 thousand patients through ABPM. However, despite the fact that Non-dipper Group had higher PP, the logistic regression model did not show association with cardiovascular events in the present study.

After the analysis of sociodemographic factors, we pointed out in our sample the absence of association between ND and the remaining variables (age, SAH time, school degree, waist circumference, genre, race, smoking and sedentarism), which was confirmed by other studies<sup>12,14,15,26</sup>. Other authors observed that individuals without ND were older<sup>16,18,19</sup> and that this condition occurs preferentially in non-white

people<sup>19</sup>. In the current study, BMI was higher in individuals without ND ( $30.9 \pm 5.7$  x  $29.2 \pm 5.0$ ,  $p = 0.0377$ ), fact also observed by Kotsis et al<sup>27</sup> in 3,216 patients without previous anti-hypertensive treatment. These authors showed a direct relation between higher BMI and higher mean pressure for ABMP, and 55% of the individuals with normal weight (normal BMI) presented ND, while only 35% of the obese individuals presented the same condition ( $p < 0.05$ ). Others, however, did not find such association<sup>12,14-16,19</sup>. In our sample, after the logistic regression model, we observed that BMI was not correlated to a higher risk for stroke or MI in ND patients.

After the biochemical dosages, we found that, except for the higher levels of HDL-c in ND patients, the remaining variables did not present statistical significance, findings that are similar to those observed in other studies<sup>15,16</sup>. Despite the lower HDL-c in non-dipper patients, there was no correlation to higher risk of lesions in target-organs. Alterations found in the levels of uric acid<sup>14,16</sup>, serum creatinine<sup>16,18</sup>, glycemia<sup>12,18</sup> and triglycerides<sup>15,16</sup> in patients without ND make their interpretation difficult due to the differences found between the studied populations as well as to the influence of medications on these biochemical parameters. Though we observed a higher prevalence of diabetic patients in the Non-dipper Group (38.2 versus 28.3%), this value was not statistically significant, which opposes to the findings of Björklund et al<sup>28</sup>, who found higher frequency of individuals without ND in a diabetic subpopulation. The homogeneous distribution of diabetes among both groups eliminates a possible confusing factor, for the presence of diabetes could interfere in the nocturnal dipping pattern. The frequent use of hypoglycemic medications in the group without ND may be explained by the presence of a greater number of

**Table 4 – Logistic regression model for stroke and MI in non-dipper patients**

Variables	$\beta$	Standard error	Odds Ratio (95%CI)	p-value
Non-dipper	11.502	0.5764	3.16 (1.02-9.78)	0.046
BMI	-0.0586	0.1022	0.94 (0.77-1.15)	NS
HDL-c	-0.00805	0.04166	0.99 (0.91-1.07)	NS
PP_s	-0.00876	0.06409	0.99 (0.87-1.12)	NS

MI - myocardium infarction; BMI - body mass index; CI - confidence interval; NS - non-significant ( $p > 0.05$ ).

diabetic patients, although there was no statistically significant difference among them.

In the current paper, stroke history ( $p = 0.046$ ) and the association with MI or stroke ( $p = 0.032$ ) were statistically significant in patients without ND. Possible reasons for these findings may be found in the history of lesions in target-organs of hypertensive patients, that is, left ventricle hypertrophy, microalbuminuria, renal dysfunction and cerebrovascular disease are more prevalent in individuals without ND<sup>1,14,18</sup>. Ohkubo et al<sup>29</sup> assessed 1,542 individuals older than 40 years old who were followed-up for approximately 9.2 years. The authors found a linear relation between nocturnal dipping of blood pressure and mortality, and each 5% of reduction of SBP and DBP drop, the risk for cardiovascular mortality would increase in 20%. Even in the presence of normal mean 24-hour pressure levels ( $\leq 130/80$  mmHg), the attenuation of nocturnal dipping of blood pressure were associated with an increase in the risk for cardiovascular death. Kario et al<sup>11</sup> followed-up a Japanese population of 575 individuals of  $\geq 50$  years old who were divided into groups according to nocturnal dipping of SBP. After a 41 months average, they observed that the incidence of stroke was of 12% among individuals with accentuate nocturnal dipping ( $\geq 20\%$ ), 6.1% among individuals with ND between 10 and 20%, 7.6% among

individuals without ND ( $\geq 0\%$  and  $< 10\%$ ) and 22% among patients with nocturnal dipping of blood pressure.

The mechanisms responsible for this abnormal variation of arterial pressure remain unknown, though there is strong evidence of a possible involvement of compromising in the autonomic balance, which leads to a sympathetic hyperactivity during sleep period that may alter circadian rhythm, common occurrence among patients with sleep apnea syndrome<sup>30</sup>. Another factor that seems to exert influence on ND phenomenon is sodium ingestion<sup>31</sup>. Some studies reported that ND would be associated to a reduced excretion of sodium during vigil period<sup>32,33</sup>. Birkenhäger and van den Meiracker<sup>34</sup> observed that a low sleep quality, along with daily inactivity, represented by sedentarism, might explain the phenomenon of ND absence.

Something that also deserves to be emphasized in our study is that mean pressure values during vigil, sleep and 24-hour period obtained by means of ABPM were above the limits recommended by our guideline<sup>1</sup>. In that case, measures as adoption of a more rigid treatment and the modification of medication administration horary could contribute with the improvement of these individuals' pressure profile and, consequently, change ND pattern<sup>35</sup>.

This previous concept that the absence of ND could be related to a worse cardiovascular and cerebral outcome has, however, exceptions and there are groups in which the influence of this variable deserves better elucidations, like in the case of individuals with previous history of cerebrovascular disease. Nakamura et al<sup>36</sup> followed-up individuals with previous stroke history and observed that ischemic event recurrence rate was higher among individuals with ND and under anti-hypertensive treatment. Besides, the frequency of new events was higher among treated hypertensive and ND patients than among those without nocturnal dipping. In that special case, though controlling pressure levels is a effective measure for the prevention of new events<sup>37</sup>, an aggressive anti-hypertensive therapy may collaborate to a cerebral hypoperfusion and, consequently, to the aggravation

**Table 5 – Prevalence of nocturnal dipping in transversal studies**

Authors	Sample composition	Number of individuals	ND prevalence
Kario et al <sup>11</sup>	Individuals with sustained hypertension and silent and/or clinically manifested stroke	575	56.8%
Anan et al <sup>12</sup>	Hypertensive patients with attenuate nocturnal dipping and high risk for cardiovascular events	103	55.3%
Torun et al <sup>14</sup>	Hypertensive individuals that never received treatment	67	64.2%
Davidson et al <sup>15</sup>	Non-diabetic individuals without use of anti-hypertensive medication	106	55.6%
Davidson et al <sup>16</sup>	Hypertensive patients with attenuate nocturnal dipping and deterioration of renal function	322	42.5%
Jerrard-Dunne et al <sup>17</sup>	Hypertensive individuals that never received treatment	314	62.7%
Brotman et al <sup>19</sup>	Hypertensive patients with attenuate nocturnal dipping and high risk for orbit due to cardiovascular events	621	42.0%
Shinohata et al <sup>21</sup>	Hypertensive individuals that never received treatment	90	60.0%

AMBPM - ambulatorial monitoring of blood pressure; ND - nocturnal dipping.

of the ischemic process, thus contributing to the development of cognitive debt<sup>38</sup>. It could happen due to the interaction between excessive pressure reduction during sleep allied to the effect of antihypertensive drugs, which could unleash cerebral ischemia and an area's infarction.

The main limitation of our study was the fact that the studied patients were divided into groups of people with and without ND based on only one 24-hour ABPM. Although some studies affirm that the characterization based only on one exam is not reliable, the accomplishment of the activities record by the patients allow us to exclude those who presented sleep disturbances due to the exam, thus eliminating possible trends. Another factor that is not less important is the fixation of a schedule and definition of vigil and sleep periods, fact confirmed by the standardization of these periods based on the time schedules defined by patients. Another limitation that must be mentioned was that we did not observe sleep apnea syndrome, which could directly influence the absence of ND<sup>39,40</sup>. However, patients who reported sleep disturbances in their daily records were excluded.

Taking into account the high cardiovascular risk and the association of risk factors in patients without nocturnal

dipping, the strict control of such factors in this group of patients is justified by the potential risk reversion. Although there are no concrete data with regard to drug treatment based on ND profile, measures such as improvement of sleep quality, reduction of sodium ingestion and better pressure control are fundamental to the minimization of cardiovascular risk due to ND absence, which contributes with a better life quality and reduction of morbidity and mortality due to SAH.

#### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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