Blunted Nocturnal Fall in Blood Pressure and Oxidative Stress in Men and Women With Essential Hypertension

Sante D. Pierdomenico, Fabrizio Costantini, Anna Bucci, Domenico De Cesare, Tonino Bucciarelli, Franco Cuccurullo, and Andrea Mezzetti

Low-density lipoprotein oxidation and antioxidant vitamins E and C were investigated in dipper (nocturnal blood pressure fall > 10%) and nondipper (nocturnal blood pressure fall < 10%) hypertensives. We studied 40 dippers and 28 nondippers balanced for gender, age, and body mass index. Blood samples were drawn for lipid profile determination, assessment of thiobarbituric acid-reactive substances, and fluorescent products of lipid peroxidation in native low-density lipoprotein, evaluation of susceptibility to low-density lipoprotein oxidation in vitro (lag phase and propagation rate), and determination of low-density lipoprotein vitamin E and plasma vitamins E and C contents. Compared with dippers, nondippers had significantly higher thiobarbituric acid-reactive substances and fluorescent products of lipid peroxidation (0.63 ± 0.1 v 0.77 ± 0.08 nmol malondialdehyde/mg low-density lipoprotein protein, and 14.5 ± 6 v 17.9 ± 4 units of relative fluorescence/mg low-density lipoprotein protein, respectively, both P < .05), shorter lag phase (56 ± 13 v 49 ± 9 min, P < .05), and lower plasma vitamin C content (42 ± 9 v 35 ± 10 μmol/L, P < .05). When gender was taken into account, differences were not significant between dipper and nondipper men, whereas, compared with dipper women, nondipper women showed significantly higher thiobarbituric acid-reactive substances and fluorescent products of lipid peroxidation (0.56 ± 0.1 v 0.77 ± 0.07 nmol malondialdehyde/mg low-density lipoprotein protein, and 12.5 ± 4 v 17.5 ± 4.6 units of relative fluorescence/mg low-density lipoprotein protein, respectively, both P < .05), shorter lag phase (62.5 ± 11 v 49 ± 9.5 min, P < .05), and lower plasma vitamin C content (44.9 ± 10 v 34.7 ± 10.8 μmol/L, P < .05). Given the role of low-density lipoprotein oxidation in the pathogenesis of atherosclerosis and that of vitamin C in protecting against it, our data suggest that nondippers, especially among women, show higher atherogenic risk than dippers.


KEY WORDS: Hypertension, dippers, nondippers, LDL oxidation, vitamin E, vitamin C.

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Ambulatory blood pressure (BP) monitoring has shown that BP is highest during the day and lowest during the night in both normotensives and hypertensives. Some hypertensives, however, exhibit a blunted nocturnal fall in BP and have been called nondippers, whereas those with a normal nocturnal drop in BP have been defined as dippers. It has been reported that, compared with dippers, nondippers have higher left ventricular mass, cerebrovascular disease, and cardiovascular morbidity. When gender was taken into account, left ventricular mass and cardiovascular morbidity were found to be significantly higher in nondippers than in dippers in women, whereas a lesser and not significant difference was observed between the two groups in men. We have recently reported that nondippers, especially among women, have greater vascular damage in the carotid arteries than dippers. Higher carotid intima-media thickness, even after adjustment for age, has also been reported by others in white nondippers with respect to dippers.

Various studies suggest that hypertension is associated with enhanced oxidative stress. Increased oxidative stress may lead to low-density lipoprotein (LDL) oxidation. It has been suggested that beyond the known risk markers for cardiovascular disease, oxidation of LDL could play an important role in the development of atherosclerosis. In addition, it may contribute to the maintenance of hypertension. There is increasing evidence that LDL is more oxidized in vivo and is more susceptible to oxidation in vitro in hypertensives than in normotensives. In this context, vitamins C and E represent the major antioxidant vitamins in the water- and lipid-soluble categories, respectively, and they protect against oxidative damage. To the best of our knowledge, apparently no study has evaluated whether dippers and nondippers show differences in LDL oxidation and antioxidant vitamins.

This study was designed to investigate LDL oxidation, evaluating lipid peroxidation products in native lipoproteins and susceptibility to oxidation in vitro, and antioxidant vitamins E and C in dipper and non-dipper hypertensives.

**MATERIALS AND METHODS**

**Subjects** We selected 40 dipper and 28 nondipper white hypertensives (see definition, later) well balanced for gender, age, and body mass index. Exclusion criteria for entry in the study were smoking habits, diabetes mellitus, hypercholesterolemia (≥ 5.7 mmol/L), hypertriglyceridemia (≥ 2.9 mmol/L), antihypertensive and lipid-lowering drug use (present or past), antioxidant substances use, known secondary hypertension, chronic renal failure, cerebrovascular disease, ischemic heart disease, congestive heart failure, and gastrointestinal and liver disease. Subjects came from the same geographical area (Chieti, Abruzzo, Italy) and had a similar dietary pattern (Mediterranean type of diet). The diet composition was assessed by a well-trained dietician who collected diet histories. The study was in accordance with the Second Declaration of Helsinki and was approved by the institutional review committee. All participating subjects gave informed consent.

**Office Blood Pressure Measurements** Clinical systolic and diastolic BP recordings were performed according to the standard technique using a mercury sphygmomanometer. Measurements were performed in triplicate, and the average value was used as the BP for the visit. Clinical hypertension was defined as systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg in three visits.

**Ambulatory Blood Pressure Monitoring** Ambulatory BP monitoring was performed with a noninvasive recorder (SpaceLabs 90207, Redmond, WA) on a day of typical activity. Technical aspects have been reported previously. Ambulatory BP readings were obtained at 15-min intervals from 6 AM to midnight, and at 30-min intervals from midnight to 6 AM. Average daytime (awake period), average nighttime (asleep period, defined as the period from falling asleep to awakening and not as time in bed), and average 24-h systolic and diastolic BP were evaluated. Awake and asleep periods were calculated from diary times. Recordings were automatically edited. Patients were arbitrarily defined as dippers when nighttime systolic and diastolic BP fall was > 10% and as nondippers when nighttime BP fall was < 10%. Patients were asked to define the quality of their sleep and only those who reported a normal sleep or a sleep like that in the previous nights were included in the study. Ambulatory hypertension was defined as daytime systolic BP ≥ 135 mm Hg or diastolic BP ≥ 85 mm Hg. Patients studied had recordings of good technical quality.

**Laboratory Procedures** Biochemical Analyses Blood samples were drawn after a fasting period of 12 h. Total cholesterol, triglycerides, and glucose were determined by standard methods. High-density lipoprotein cholesterol was measured by immunoturbidimetric technique; LDL cholesterol was calculated by Friedewald’s formula.

**LDL Isolation** The LDL fraction was isolated as reported and dialyzed for 22 h in the dark against three changes of PBS containing EDTA (10 μmol/L), pH 7.4, at 4°C. LDL cholesterol was measured by an enzymatic reagent (CHOD-PAP MPRI, Boehringer...
Mannheim) and LDL protein was determined by the method of Lowry et al.38

**LDL Oxidation** Oxidation of LDL (fresh preparations at a concentration of 0.2 mg LDL cholesterol/mL) was triggered by the addition of 5 µmol/L CuSO₄ in PBS, pH 7.4, at 37°C and continuously monitored spectrofluorometrically at 234 nm to evaluate the formation of conjugated dienes.39 The oxidation curve is characterized by the lag phase, the propagation phase, and the decomposition phase.39 The lag phase and the propagation rate were calculated as previously reported.39 Two LDL preparations of the same sample were oxidized in two consecutive oxidation runs on the same day. The values reported for lag phase and propagation rate are means of the values thus obtained. The coefficients of variation for lag phase and propagation rate were 3.1% and 3.8%, respectively.

**Lipid Peroxidation in Native LDL** Lipid peroxidation in native LDL was evaluated by the assessment of two indexes: thiobarbituric acid-reactive substances (TBARS) and fluorescent products of lipid peroxidation (FPLP). TBARS mainly reflect malondialdehyde content in LDL35; they are widely used for the evaluation of lipid peroxidation although some reservations exist about their specificity.35 TBARS were evaluated as previously reported.29 Fluorescent reaction products were assayed spectrofluorometrically at 515 nm excitation and 553 nm emission (Kontron SFM 25 spectrofluorometer, Milan, Italy), by Yagi’s method.40 Freshly diluted tetramethoxypropane, which yields malondialdehyde, was used as a standard and results were expressed as nmol malondialdehyde/mg LDL protein. FPLP essentially reflect the interaction of polyunsaturated fatty acid peroxidation products with amino groups of phospholipids and apolipoprotein B.35,41–45 They are more sensitive and specific than TBARS and tend to remain localized at the site of oxidant burden.44 The samples were irradiated with ultraviolet light to remove the fluorescence contribution of such compounds as retinol just before fluorimetric measurements. Fluorescence was estimated spectrofluorometrically at 360 nm excitation and 430 nm emission using a Kontron SFM 25 spectrofluorometer calibrated with quinine sulphate and results were expressed as units of relative fluorescence/mg LDL protein. The 430-nm fluorescence in freshly prepared LDL is indicative of remnants of in vivo lipid peroxidation.35 TBARS and FPLP were evaluated twice from the same sample on the same day. The data reported are means of the values thus obtained. The coefficients of variation for TBARS and FPLP were 3.6% and 3.1%, respectively.

**Vitamin E and Vitamin C Determination** LDL and plasma vitamin E were measured with high-perfor-

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**TABLE 1. CHARACTERISTICS AND BLOOD PRESSURE VALUES OF STUDY POPULATION**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dippers</th>
<th>Nondippers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>40</td>
<td>28</td>
</tr>
<tr>
<td>Men/women</td>
<td>20/20</td>
<td>14/14</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46 ± 8</td>
<td>47 ± 9</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.6 ± 3.1</td>
<td>26.8 ± 3.1</td>
</tr>
<tr>
<td>Sleep duration (h)</td>
<td>6.5 ± 0.7</td>
<td>6.2 ± 0.9</td>
</tr>
<tr>
<td>Clinical SBP (mm Hg)</td>
<td>150 ± 4</td>
<td>152 ± 8</td>
</tr>
<tr>
<td>Clinical DBP (mm Hg)</td>
<td>98 ± 3</td>
<td>99 ± 4</td>
</tr>
<tr>
<td>Daytime SBP (mm Hg)</td>
<td>147 ± 10</td>
<td>149 ± 7</td>
</tr>
<tr>
<td>Daytime DBP (mm Hg)</td>
<td>95 ± 7</td>
<td>96 ± 6</td>
</tr>
<tr>
<td>Nighttime SBP (mm Hg)</td>
<td>125 ± 11</td>
<td>138 ± 6</td>
</tr>
<tr>
<td>Nighttime DBP (mm Hg)</td>
<td>76 ± 9</td>
<td>88 ± 6</td>
</tr>
<tr>
<td>24-h SBP (mm Hg)</td>
<td>141 ± 10</td>
<td>147 ± 7</td>
</tr>
<tr>
<td>24-h DBP (mm Hg)</td>
<td>90 ± 8</td>
<td>94 ± 5</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure. *P < .05 versus dippers.

**Statistical Analysis** Data are expressed as means ± SD. Dipper and nondipper groups were compared with unpaired Student’s t test.48 Comparisons between groups by gender were performed using two-way ANOVA followed by Scheffe’s test for multiple comparisons.48 ANCOVA was also used when needed. Analyses were made with the SYSTAT program on an Apple (Cuppertino, CA) Macintosh SE/30 personal computer. Statistical significance was defined as P < .05.

**RESULTS**

Characteristics and BP values of the study population are reported in Table 1. Age, gender distribution, body mass index, sleep duration, and clinical and daytime BP were similar between the groups. Nighttime and 24-h BP were significantly higher in nondippers than in dippers.

Menopausal status was not different between dippers and nondippers. Indeed, 12 (60%), one (5%), and seven (35%) dippers and eight (57%), two (14%), and four (29%) nondippers were in premenopausal, perimenopausal, and postmenopausal status, respectively. One dipper and one nondipper postmenopausal women were taking hormonal replacement therapy.
were teachers. Among dipper women, 14 (70%) were employees, three (15%) were teachers, and three (15%) were housewives, and among nondipper women, 10 (72%) were employees, two (14%) were teachers, and two (14%) were housewives. Both male and female employees had largely sedentary jobs. The analysis of patients’ diaries showed that, during the daytime, there was no difference between dippers and nondippers concerning work, home, and rest time.

Laboratory findings are reported in Table 2. Glucose, total cholesterol, high-density lipoprotein cholesterol, triglycerides, and LDL cholesterol were similar between groups as a result of the selection process. TBARS and FPLP contents in native LDL were significantly higher in nondippers than in dippers. Lag phase was significantly shorter in nondippers than in dippers. Propagation rate, LDL vitamin E, and plasma vitamin E contents were not significantly different between groups. Plasma vitamin C was significantly lower in nondippers than in dippers.

Separate results for men and women are reported in Table 3. Age and total and LDL cholesterol were similar among groups. Nighttime BP was significantly higher in nondippers than in dippers in both men and women. Twenty-four–hour BP was higher in nondippers than in dippers in both men and women but did not attain statistical significance because of the smaller numbers. LDL oxidation measures and vitamins did not differ significantly between dipper and nondipper men, whereas nondipper women showed significantly higher TBARS and FPLP contents in native LDL, shorter lag phase, and lower plasma vitamin C than dipper women. Moreover, dipper women had signifi-

### Table 2. Laboratory Findings of Study Population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dippers</th>
<th>Nondippers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mmol/L)</td>
<td>4.6 ± 0.3</td>
<td>4.65 ± 0.3</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.06 ± 0.72</td>
<td>4.99 ± 0.62</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.29 ± 0.18</td>
<td>1.24 ± 0.25</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.25 ± 0.57</td>
<td>1.34 ± 0.68</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.25 ± 0.54</td>
<td>3.13 ± 0.44</td>
</tr>
<tr>
<td>TBARS (nmol MDA/mg LDL-P)</td>
<td>0.63 ± 0.1</td>
<td>0.77 ± 0.08*</td>
</tr>
<tr>
<td>FPLP (URF/mg LDL-P)</td>
<td>14.5 ± 6</td>
<td>17.9 ± 3.9*</td>
</tr>
<tr>
<td>Lag phase (min)</td>
<td>56 ± 13</td>
<td>49 ± 9*</td>
</tr>
<tr>
<td>PR (nmol diene/min/mg LDL-C)</td>
<td>7.7 ± 3.1</td>
<td>8.0 ± 3.2</td>
</tr>
<tr>
<td>LDL vitamin E (nmol/mg LDL-C)</td>
<td>8.5 ± 1.1</td>
<td>8.3 ± 0.9</td>
</tr>
<tr>
<td>Plasma vitamin E (nmol/L)</td>
<td>25.5 ± 3.7</td>
<td>25.7 ± 3.5</td>
</tr>
<tr>
<td>Plasma vitamin C (µmol/L)</td>
<td>42 ± 9</td>
<td>35 ± 10*</td>
</tr>
</tbody>
</table>

HDL, high-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; MDA, malondialdehyde; LDL-P, low-density lipoprotein; URF, units of relative fluorescence; PR, propagation rate.

* P < .05 versus dippers.

### Table 3. Age, Ambulatory Blood Pressure, and Main Laboratory Findings of Study Populations by Gender

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46 ± 8</td>
<td>47 ± 9</td>
<td>46 ± 9</td>
<td>47 ± 9</td>
</tr>
<tr>
<td>Daytime BP (mm Hg)</td>
<td>148 ± 8/95 ± 7</td>
<td>149 ± 9/96 ± 4</td>
<td>146 ± 11/95 ± 7</td>
<td>148 ± 4/96 ± 6</td>
</tr>
<tr>
<td>Nighttime BP (mm Hg)</td>
<td>125 ± 9/76 ± 6</td>
<td>140 ± 7/88 ± 3*</td>
<td>124 ± 13/76 ± 11</td>
<td>136 ± 3/87 ± 7*</td>
</tr>
<tr>
<td>24-h BP (mm Hg)</td>
<td>142 ± 9/90 ± 7</td>
<td>147 ± 8/94 ± 4</td>
<td>140 ± 11/90 ± 9</td>
<td>147 ± 4/94 ± 6</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.1 ± 0.82</td>
<td>5.1 ± 0.75</td>
<td>5.04 ± 0.56</td>
<td>4.86 ± 0.69</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.31 ± 0.54</td>
<td>3.2 ± 0.38</td>
<td>3.15 ± 0.51</td>
<td>3.07 ± 0.46</td>
</tr>
<tr>
<td>TBARS (nmol MDA/mg LDL-P)</td>
<td>0.69 ± 0.1</td>
<td>0.77 ± 0.07</td>
<td>0.56 ± 0.1*</td>
<td>0.77 ± 0.07*</td>
</tr>
<tr>
<td>FPLP (URF/mg LDL-P)</td>
<td>16.0 ± 5.7</td>
<td>18.3 ± 2.5</td>
<td>12.5 ± 4*</td>
<td>17.5 ± 4.6*</td>
</tr>
<tr>
<td>Lag phase (min)</td>
<td>50 ± 13</td>
<td>48 ± 7.9</td>
<td>62.5 ± 11</td>
<td>49 ± 9.5*</td>
</tr>
<tr>
<td>PR (nmol diene/min/mg LDL-C)</td>
<td>8.1 ± 3</td>
<td>8.2 ± 2</td>
<td>7.2 ± 2</td>
<td>7.8 ± 3</td>
</tr>
<tr>
<td>LDL vitamin E (nmol/mg LDL-C)</td>
<td>8.3 ± 1.1</td>
<td>8.3 ± 1</td>
<td>8.6 ± 1.1</td>
<td>8.4 ± 0.9</td>
</tr>
<tr>
<td>Plasma vitamin E (µmol/L)</td>
<td>25 ± 4</td>
<td>25.1 ± 2.9</td>
<td>25.9 ± 3</td>
<td>26.2 ± 3.9</td>
</tr>
<tr>
<td>Plasma vitamin C (µmol/L)</td>
<td>39.2 ± 8</td>
<td>35.3 ± 11</td>
<td>44.9 ± 10</td>
<td>34.7 ± 10.8*</td>
</tr>
</tbody>
</table>

LDL-C, low-density lipoprotein cholesterol; MDA, malondialdehyde; LDL-P, low-density lipoprotein; URF, units of relative fluorescence; PR, propagation rate.

* P < .05 versus dippers of the same gender; † P < .05 versus dipper men.
Antioxidant Vitamins

Vitamin E is the major antioxidant that scavenges lipid peroxyl radicals,\(^35\) both in lipoproteins and cellular membranes. We have found a similar LDL vitamin E content in dippers and nondippers, both before and after gender was taken into account. Concentration of vitamin E in LDL is the result of exogenous intake, its transfer from LDL to cellular membranes or other lipoproteins, and its metabolic redox reactions in LDL.\(^45\) It can be hypothesized that although LDL vitamin E could be more frequently oxidized in nondippers, it could be promptly regenerated by other antioxidant systems, such as vitamin C. Indeed, it has been reported that vitamin C can both preserve\(^50\) and regenerate\(^45\) vitamin E.

Vitamin C is a water-soluble chain-breaking antioxidant that reacts with oxygen-free radicals.\(^34\) It represents the outstanding antioxidant in plasma,\(^34\) prevents vascular-cell-mediated LDL oxidation,\(^51\) and can regenerate vitamin E from the radical form.\(^45\) Moreover, some studies have shown a negative correlation between BP and vitamin C.\(^52-55\) Various mechanisms by which vitamin C might influence BP have been proposed,\(^55\) including a free radical scavenging property preventing prostacyclin synthetase inhibition.\(^53\) In addition, it has also been suggested that BP may influence vitamin C metabolism.\(^52,55\) We have found lower levels of vitamin C in nondippers than in dippers. It can be speculated that the lower vitamin C level found in nondippers may be the result of a greater antioxidant consumption in response to an increased oxidative stress associated with pressure overload over 24 h.

Gender-Related Differences

As mentioned, the differences observed in the present study were less evident between dipper and nondipper men and more evident between dipper and nondipper women. It is intriguing to attempt to explain these findings. Recent studies suggest that estrogens inhibit oxidative modification of LDL,\(^56-59\) whereas testosterone does not\(^57\) or could have prooxidant activity.\(^59\) Thus, sex steroids could influence LDL oxidation in biologic systems. It can be speculated that in hypertensive men, because of the lack of a protective effect of androgens or because of their prooxidant activity, the oxidative stress could be shifted towards higher levels during the daytime with a consequently small, although present, additive effect of elevated nighttime BP. In hypertensive women, owing to the protective effect of estrogens, oxidative stress could be blunted during the daytime and they could need a longer exposure to high BP throughout 24 h to overwhelm estrogen’s protective effect and experience higher oxidative stress. Some differences observed between dipper men and dipper women, but not between nondipper men and nondipper women, could contribute to support this hypothesis. In addition, it can also be speculated that nondipper women, compared with dipper women, show reduced activity of other antioxidant systems not evaluated in the present study.

Pathophysiologic Implications

We have recently reported\(^16\) greater vascular damage in the carotid arteries (atherosclerotic plaques and intima-media thickness) in nondippers than in dippers in women and a lesser and not significant difference between the two
groups in men. Higher carotid intima-media thickness, even after adjustment for age, has also been reported by others\textsuperscript{17} in white nondippers in comparison with dippers. The association between LDL oxidation and atherosclerotic plaques seems clear. Whether in hypertensive patients increased intima-media thickness is a sign of early atherosclerosis\textsuperscript{60} or of hypertension-induced vascular hypertrophy\textsuperscript{61} is unclear. However, both these phenomena could be present. Increased oxidative stress could both lead to atherogenesis and contribute to vessel wall hypertrophy by its influence on growth factors.\textsuperscript{62,63} In this context, our findings, especially among women, could help to explain previous reports.\textsuperscript{16,17}

It is not yet clear whether enhanced oxidative stress occurs before or after the development of hypertension.\textsuperscript{18–26} In the former hypothesis, our data suggest that dippers and nondippers could show some differences in pathophysiologic background. In the latter hypothesis, our results suggest that pressure overload throughout 24 h is associated with enhanced oxidative stress and increased LDL oxidation.

**Study Limitations** First, because of the complexity of our procedures we could not obtain a larger sample size. This problem arises especially when dippers and nondippers are analyzed by gender, leading to even smaller groups. Thus, it cannot totally be excluded that the lack of a significant difference between dipper and nondipper men may be due to a type II error. In any case, our data suggest that differences between dippers and nondippers are far more evident in women than in men. Second, because smoking habits, diabetes, and dyslipidemia are associated with increased LDL oxidation independently of BP values, we excluded subjects with these characteristics. Whether the impact of 24-h BP profile on LDL oxidation and plasma vitamin C could be different in sustained hypertensives with other additional risk factors should be determined. Third, whether differences between men and women according to circadian BP profile persist when only hypertensive women far along in postmenopausal status are studied should also be evaluated. Fourth, Pickering and James\textsuperscript{64} have recently proposed that dippers and nondippers could be better defined as peakers and nonpeakers, respectively, considering the sleep BP as the baseline level and awake BP as the result of various extrinsic factors. Regardless of the definition, however, our data suggest that nondipper/nonpeaker women show increased oxidative stress with respect to dipper/peaker ones. Fifth, it could be argued that, in nondippers, increased oxidative stress may be the result of higher 24-h BP and not of circadian BP pattern. Differences observed between dippers and nondippers remained significant after adjustment for 24-h BP, suggesting that circadian BP pattern, together with higher 24-h BP, could contribute to increased oxidative stress. This aspect, however, should be interpreted with caution because, as mentioned, it is not yet clear whether increased oxidative stress precedes or follows hypertension. Last, our conclusions may not be extended to other racial groups.

**Conclusions** Given the role of LDL oxidation in the pathogenesis of atherosclerosis and that of vitamin C in protecting against it, our data suggest that nondippers, especially among women, show higher atherogenic risk than dippers.

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