Blunted Nocturnal Fall in Blood Pressure and Left Ventricular Mass in Elderly Individuals With Recently Diagnosed Isolated Systolic Hypertension

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Background: Few studies have investigated the relationship between the lack of or reduction of nocturnal blood pressure (BP) fall and left ventricular mass (LVM) in elderly individuals with isolated systolic hypertension (ISH), notwithstanding the fact that ISH is the most frequent subtype of uncontrolled hypertension and a powerful risk factor for organ damage. The aim of this study was to identify the relationship between blunted nocturnal BP fall and LVM in elderly individuals with ISH that was recently diagnosed (within 2 years) and had never been treated.

Methods: A total of 64 elderly patients with recent ISH were recruited among the outpatients of the Hypertension Unit at 1st Institute of Medicine of “La Sapienza” University in Rome, and they underwent 24-h ambulatory BP monitoring (ABPM). According to exclusion criteria, 37 patients were selected for the study. Based on the presence or absence of an almost 10% reduction in systolic BP (SBP) and diastolic BP (DBP) from day to night, 21 so-called dippers and 16 nondippers, respectively, were identified. All of these 37 patients underwent echocardiography. Relationships between BP recordings and echocardiographic parameters were assessed by univariate analysis. Dippers and nondippers were compared with respect to LVM.

Results: Nighttime SBP was closely associated with indexed LVM (LVM/h^2.7) (r = 0.564; P < .001). Nondippers showed significantly higher LVM/h^2.7 compared with dippers (62.43 ± 15.39 g/m^2.7 vs 51.33 ± 12.68 g/m^2.7 respectively; P = .021).

Conclusions: An association between blunted nocturnal SBP fall and increased LVM was observed in the early phases of ISH in the elderly. This finding may have important prognostic implications.

Key Words: Elderly, isolated systolic hypertension, dippers and nondippers, left ventricular mass.

The circadian pattern of blood pressure (BP) can easily be detected by 24-h ambulatory BP monitoring (ABPM) showing a nocturnal BP fall of at least 10% in most subjects (the so-called “dippers”). In other subjects (the “nondippers”), BP behavior is characterized either by the lack of a nocturnal BP fall or by a reduction in this fall.1

The nondipping pattern has been observed in many conditions (malignant and secondary hypertension, diabetes, autonomic neuropathies, sleep apnea syndrome) and also in essential hypertension.2 Several cross-sectional studies have suggested that the nondipping pattern is more frequently associated with left ventricular hypertrophy (LVH) compared with the dipping pattern,3 whereas other authors have not confirmed this finding.4 This discrepancy may be due to differences in duration or severity of hypertensive status as well as to differences in pharmacologic therapy.

Few studies have investigated the relationship between the lack of or reduction of nocturnal BP fall and left ventricular mass (LVM) in elderly individuals with isolated systolic hypertension (ISH), notwithstanding the fact...
that ISH is the most frequent subtype of uncontrolled hypertension. However, identification of the relationship between a reduced nocturnal BP fall and LVM is important, because in uncomplicated hypertension there is a continuous relation between LVM and the risk of cardiovascular disease over a wide range of LVM values, and systolic BP (SBP) has been demonstrated to be the main determinant of LVM.7

Thus, the aim of this study was to compare the echocardiographic findings between elderly dippers and nondippers with recently (within <2 years) diagnosed and never previously treated ISH, to evaluate the relationship between the blunted nocturnal BP fall and LVM in the early phases of ISH.

Methods
Patients and BP Measurements
Starting January 1, 2002, a total of 166 new elderly patients with diagnoses of arterial hypertension according to World Health Organization guidelines8 were seen at our Hypertension Unit. From this series, 64 patients with recently diagnosed (within <2 years), never treated ISH (clinic systolic BP [SBP] between 140 and 179 mm Hg and clinic diastolic BP [DBP] <90 mm Hg) were recruited for the study. Patients were excluded if they were affected by the following: cerebrovascular and other neurologic diseases; sleep disturbances (insomnia, sleep apnea syndrome); atrial fibrillation, heart valve, or coronary artery disease, congestive heart failure, carotid artery stenosis >50%; liver, respiratory or kidney disease; diabetes, endocrinologic disease; obesity; neoplasm; secondary hypertension or postural hypotension; autonomic dysfunction; or tobacco use or alcohol abuse.

Body mass index (BMI) was calculated as weight (in kilograms) divided by the height squared (in meters). Body surface area (BSA) was calculated as (0.0001 kg/m²/cm)0.425 (cm)0.725. For a 2-week period the patients followed a normal sodium diet containing approximately 10 g of NaCl per day. Compliance with the prescribed sodium intake was assessed by a 24-h urinary sodium excretion measurement. Clinic measurements of BP were made by a member of our medical staff according to WHO guidelines.8

All patients underwent 24-h ABPM, performed during a work day (Monday to Friday), using an automatic portable BP monitor A&D TM 2421 device according to recommendations of the British Hypertension Society.10 The ABPM measurements were performed with the oscillometric method every 15 min in daytime (from 8 AM to 10 pm) and every 20 min in nighttime (from 10 PM to 8 AM). The patients kept a diary of daily activities and bedtime; in particular, the patients were asked to note the disruption to normal sleep caused by ABPM and the number of nighttime awakenings caused by the need to urine. The patients who noted a sleep time different from the bedtime and a bedtime different from the nighttime,11 sleeping disturbances,12 or unusual events or naps during the day13 were excluded from the study.

Based on the previously mentioned exclusion criteria, 27 patients were excluded from the study. In particular, 13 patients were excluded for comorbidities, four patients did not follow the prescribed daily sodium intake, five patients had repeated nighttime awakenings, three patients had disruption to normal sleep caused by ABPM, and two patients took naps.

In all, 37 elderly individuals with ISH were selected. Day and night were calculated using the so-called “narrow fixed clock” intervals (day from 10 AM to 8 PM; night from 12 midnight to 6 AM).14 Average SBP and DBP were calculated. These parameters were assessed for either the daytime or nighttime or for 24 h. Nondippers and dippers were identified on the basis of a <10% reduction in SBP and DBP from day to night, respectively.15 The percent reduction in nocturnal BP was calculated as (daytime BP – nighttime BP) × 100/daytime BP and nocturnal BP dipping as (1 – sleep BP/awake BP).

Echocardiographic Study
M-mode echocardiographic tracings were performed with commercially available equipment. The tracings were obtained with the patients in partial left decubitus position, and images were stored on VHS videotape. Left ventricular dimensions were measured in parasternal long-axis view at end-diastole and end-systole according to American Society of Echocardiography (ASE) recommendations.16 The LVM was calculated according to the Penn convention,17 and was normalized by the height in meters and elevated to the power of 2.7 as LVM/h².27,19 Relative wall thickness (RWT) was calculated as 2 × PWT/LVDD.20 Patterns of left ventricular geometry were defined according to Ganau et al.,20 as left ventricular concentric remodeling, concentric LVH, or eccentric LVH. Echocardiographic examinations were performed by the same experienced sonographer, and the reading of the tracings was made in casual order by two physicians blinded to the clinical data; discrepancies were resolved by consensus. Only frames with optimal visualization of left ventricular interfaces and showing simultaneous visualization of interventricular septal thickness, posterior wall thickness, and left ventricular internal dimension in the whole cardiac cycle were considered for reading.21 The values from five consecutive cardiac cycles were averaged for calculations.

The study was conducted in accordance with the Declaration of Helsinki, and all patients gave their informed consent.

Statistical Analysis
Blood pressure, echocardiographic left ventricular and atrial dimensions, and demographic and anthropometric
Table 1. Age, sex, body mass index (BMI), body surface area (BSA), clinic and ambulatory blood pressure (BP) and heart rate (HR) values in all 37 patients and in dippers versus nondippers

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Dippers</th>
<th>Nondippers</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>70.81 ± 8.95</td>
<td>70.19 ± 9.09</td>
<td>71.62 ± 8.99</td>
<td>.635</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>15/22</td>
<td>8/13</td>
<td>7/9</td>
<td>.749</td>
</tr>
<tr>
<td>Gender (male %)</td>
<td>40.5</td>
<td>38</td>
<td>44</td>
<td>.749</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.98 ± 2.86</td>
<td>24.34 ± 3.18</td>
<td>25.82 ± 2.19</td>
<td>.122</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.65 ± 0.14</td>
<td>1.67 ± 0.17</td>
<td>1.62 ± 0.09</td>
<td>.297</td>
</tr>
<tr>
<td>Clinic SBP (mm Hg)</td>
<td>157.06 ± 13.9</td>
<td>159.76 ± 15.43</td>
<td>153.53 ± 9.47</td>
<td>.164</td>
</tr>
<tr>
<td>Clinic DBP (mm Hg)</td>
<td>83.81 ± 6.98</td>
<td>83.71 ± 7.79</td>
<td>83.93 ± 6.00</td>
<td>.924</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>67.55 ± 8.42</td>
<td>67.52 ± 8.80</td>
<td>67.58 ± 8.18</td>
<td>.985</td>
</tr>
<tr>
<td>24h SBP (mm Hg)</td>
<td>144.62 ± 15.17</td>
<td>143.80 ± 16.86</td>
<td>145.69 ± 13.07</td>
<td>.714</td>
</tr>
<tr>
<td>24h DBP (mm Hg)</td>
<td>77.18 ± 7.98</td>
<td>77.19 ± 5.76</td>
<td>77.17 ± 10.43</td>
<td>.995</td>
</tr>
<tr>
<td>24h HR (beats/min)</td>
<td>68.59 ± 9.37</td>
<td>68.50 ± 10.23</td>
<td>68.70 ± 8.43</td>
<td>.949</td>
</tr>
<tr>
<td>Daytime SBP (mm Hg)</td>
<td>146.25 ± 15.57</td>
<td>146.31 ± 18.12</td>
<td>146.17 ± 12.00</td>
<td>.979</td>
</tr>
<tr>
<td>Daytime DBP (mm Hg)</td>
<td>79.13 ± 8.23</td>
<td>79.94 ± 6.23</td>
<td>78.07 ± 10.42</td>
<td>.500</td>
</tr>
<tr>
<td>Daytime HR (beats/min)</td>
<td>70.24 ± 9.29</td>
<td>70.31 ± 10.09</td>
<td>70.14 ± 8.46</td>
<td>.955</td>
</tr>
<tr>
<td>Nighttime SBP (mm Hg)</td>
<td>131.46 ± 17.66</td>
<td>123.08 ± 14.24</td>
<td>142.46 ± 15.82</td>
<td>.0004</td>
</tr>
<tr>
<td>Nighttime DBP (mm Hg)</td>
<td>70.24 ± 9.11</td>
<td>66.45 ± 5.33</td>
<td>75.21 ± 10.72</td>
<td>.0069</td>
</tr>
<tr>
<td>Nighttime HR (beats/min)</td>
<td>61.13 ± 9.20</td>
<td>60.20 ± 9.60</td>
<td>62.36 ± 8.80</td>
<td>.485</td>
</tr>
</tbody>
</table>

Data were synthesized using means and standard deviations or frequencies. Differences between patterns (dipping versus nondipping) were analyzed by the Student’s t test for independent groups. In addition, to assess the effect of the pattern on LVMI while simultaneously taking into account differences between patients regarding BMI and gender, analysis of covariance was applied, considering pattern as a grouping factor and BMI and gender as covariates.

Differences between clinic and ABPM measurements were analyzed by the Student paired t test. Correlations between variables were assessed by the Pearson linear correlation coefficient. Percentage differences of the different left ventricular geometry between the two groups were analyzed by the χ² test. Statistical analyses were performed using the SPSS Statistical Package (Dynamic Release 9.0, SPSS Inc., Chicago, IL) and BMDP Package (Dynamic Release 7.0, 1997, Los Angeles, CA).

Results

Demographic and anthropometric data, clinic and ambulatory BP values, and echocardiographic parameters for the 37 study subjects are shown in Tables 1 and 2. All ambulatory BP values were significantly lower than clinic BP values; in particular, 24-h SBP levels were on average 12.4 mm Hg lower than clinic SBP (P < .000), and daytime SBP levels were on average 10.8 mm Hg lower than clinic SBP (P = .000).

At univariate analysis, LVMI was associated with nighttime SBP (r = 0.564; P = .001) 24-h SBP (r = 0.453; P = .005), daytime SBP (r = 0.401; P = .014), and nocturnal SBP dipping (r = −0.393; P = .016) (Fig. 1). An association was found between RWT and clinic SBP (r = 0.412; P = .011).

Among 37 subjects, 22 (59 %) had LVH as defined by LVMI > 51 g/m². In addition, 16 subjects had <10% reduction in BP from day to night and were classified as nondippers, and the remaining 21 subjects were classified as dippers. The dippers and nondippers were well matched with regard to age, sex, BMI, and BSA (Table 1). No significant differences in SBP and DBP values were found between dippers and nondippers with respect to clinic, 24-h, and daytime BP values, whereas nighttime BP val-

Table 2. Echocardiographic parameters in all 37 patients and in dippers and nondippers

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Dippers</th>
<th>Nondippers</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVIDD (mm)</td>
<td>46.69 ± 5.92</td>
<td>45.24 ± 5.30</td>
<td>48.50 ± 6.31</td>
<td>.101</td>
</tr>
<tr>
<td>IVST (mm)</td>
<td>10.70 ± 2.10</td>
<td>10.99 ± 2.28</td>
<td>10.47 ± 1.87</td>
<td>.468</td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>9.91 ± 1.89</td>
<td>9.53 ± 2.21</td>
<td>10.39 ± 1.30</td>
<td>.179</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>200.07 ± 50.54</td>
<td>186.26 ± 38.46</td>
<td>218.21 ± 59.51</td>
<td>.055</td>
</tr>
<tr>
<td>LVM/h².⁷ (g/m².⁷)</td>
<td>56.13 ± 14.80</td>
<td>51.33 ± 12.68</td>
<td>62.43 ± 15.39</td>
<td>.021</td>
</tr>
<tr>
<td>RWT</td>
<td>0.43 ± 0.13</td>
<td>0.43 ± 0.17</td>
<td>0.43 ± 0.06</td>
<td>.920</td>
</tr>
<tr>
<td>LA (mm)</td>
<td>37.73 ± 5.78</td>
<td>36.95 ± 6.64</td>
<td>38.85 ± 4.24</td>
<td>.351</td>
</tr>
<tr>
<td>LA/AR</td>
<td>1.14 ± 0.22</td>
<td>1.11 ± 0.24</td>
<td>1.18 ± 0.19</td>
<td>.397</td>
</tr>
</tbody>
</table>

IVST = interventricular septal thickness; LA = left atrial diameter; LA/AR = left atrial diameter/aortic root; LVIDD = left ventricular internal diameter at end diastole; LVM = left ventricular mass; LVM/h².⁷ = left ventricular mass/height².⁷; PWT = posterior wall thickness; RWT = relative wall thickness.
ues were significantly different between the two groups (Table 1).

There were no significant differences between the two groups with regard to echocardiographic left ventricular and atrial dimensions or the RWT and LVM, whereas LVM/h².⁷ was significantly higher (P = .021) in nondipper hypertensive subjects (Table 2). When adjusting for BMI and sex, the difference in LVM/h².⁷ was still present, although not quite significant (adjusted means: dippers, 52.54; nondippers, 60.85; P = .0781). When considering BMI as the only covariate (inasmuch as sex did not seem to significantly affect LVM/h².⁷ values [P = .1538]), the significance level of nocturnal BP pattern did improve (adjusted means: dippers, 52.58; nondippers, 61.19; P = .0623).

No significant differences were found between dippers and nondippers with regard to the prevalence of left ventricular concentric remodeling, whereas the prevalence of subjects with LVH was significantly higher among the nondippers than among dippers (81% vs 43%, respectively; P = .002). Eccentric hypertrophy was the most frequent type of LVH in both nondippers and dippers.

**Discussion**

In this study, elderly individuals with ISH showed ambulatory SBP values higher than normal limits, as reported in a large, population-based, epidemiological study. The 24-h SBP, daytime SBP and nighttime SBP values were found to be related to LVM/h².⁷. However LVM/h².⁷ was more strictly associated with nighttime SBP levels. This finding is in agreement with the Systolic Hypertension in Europe (SYST-EUR) Trial results, which showed that cardiac endpoints were predicted only by nighttime SBP.

According to previously reported linear associations between age and LVM, the prevalence of LVH that we observed was 59%. Few studies have investigated the echocardiographic findings in elderly individuals with ISH, often including only small samples of subjects with ISH as well as varying selection criteria and different normalization criteria for LVM. The prevalence of LVH ranged from 26% in the Systolic Hypertension in the Elderly Program (SHEP) Trial to 66% in the recently published Losartan Intervention For Endpoint Reduction (LIFE) study. None of these studies investigated the relationship between LVM and circadian BP pattern in elderly patients with ISH.

In our study the prevalence of nondippers was 43% (16 of 37 cases), similar to previous studies. Although no differences were seen between dippers and nondippers with regard to 24-h ambulatory BP findings including SBP, which has been reported as the main determinant of LVH, the LVM/h².⁷ was significantly (P = .021) higher in nondippers. Analysis of covariance shows that the observed differences of LVM/h².⁷ between the two groups may be affected by the BMI but cannot be completely attributed to BMI. Therefore, the analysis of covariance seems to confirm that the increase in LVM/h².⁷ is related to the nondipping pattern.

The significant association of LVM/h².⁷ with nighttime SBP values is in agreement with significantly higher LVM/h².⁷ in nondippers, indicating that a blunted nocturnal SBP may favor the progression to LVH in early phases of ISH in elderly persons. This is confirmed by the significantly higher prevalence of LVH in nondippers.

Some studies have already investigated the relationship between blunted nocturnal BP fall and LVM in elderly individuals with systo-diastolic hypertension (SDH), and have detected a relationship between nighttime BP and LVM and between a greater nocturnal BP fall and lower LVM. However, these studies recruited elderly persons with SDH and not with ISH, with different duration and severity of hypertension, and in some cases hypertension that was already pharmacologically treated. Other more recent studies, confirmed these findings in young patients with new onset, never treated SDH. Ferrara et al. in 11 nondippers compared with 45 dippers with newly (<1 yr) discovered hypertension, found a significant change in cardiac structure similar to that found in patients with long-standing hypertension. Cuspidi et al. in 26 nondippers and 92 dippers, defined by two sessions of 24-h ABPM, with recent (<2 years) SDH and similar 24-h BP values, showed a higher prevalence of LVH in nondippers.

Several limitations of our study should be considered. The study population is small. However, carefully selecting and recruiting elderly individuals with recently diagnosed, never treated ISH is objectively difficult. Furthermore, the patients were classified as dippers or nondippers on the basis of a single 24-h ABPM, although some studies have found that day–night SBP differences in elderly persons and classification of patients as dippers and nondippers are poorly reproducible over time. However we have improved the reproducibility of the circadian SBP pattern and have ensured a better reliability of the assessment of dipping and nondipping patterns with...
a careful selection of study subjects and by using the diary and the “narrow-fixed clock” intervals. On the other hand, the two study groups fulfilled all of the criteria normally used to define dipping and nondipping patterns: the dippers showed an absolute day-night SBP difference of >10 mm Hg, and the nondippers a difference of <10 mm Hg; the night/day SBP ratio was <0.90 in the dippers (0.84 ± 0.03) and higher in the nondippers (0.97 ± 0.04).

In conclusion, in this study we observed an association between blunted nocturnal SBP fall and increased LVM already in the early phases of ISH in the elderly individuals studied. This finding may have important prognostic implications. An assessment of nocturnal BP pattern by 24-h ABPM should perhaps be included as part of the risk stratification in elderly persons with ISH. Further studies with a larger sample size and repeated ambulatory BP measurements are needed before any practical conclusions can be reached.

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References


