Ambulatory Blood Pressure and Cardiac Rhythm Disturbances in Elderly Hypertensives: Relation to Left Ventricular Mass and Filling Pattern

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Summary
In order to define cardiac hypertensive involvement a group of 25 consecutive elderly male hypertensive outpatients and 25 age-matched male normotensive controls underwent full non-invasive assessment of cardiac status by resting 12-lead electrocardiography, Doppler-echocardiographic examination and simultaneous ambulatory blood pressure and electrocardiographic monitorings. Elderly hypertensives showed a higher prevalence of electrocardiographic left ventricular hypertrophy, an increased echocardiographic left ventricular mass, an impaired left ventricular filling pattern and more frequent ventricular arrhythmias when compared with normotensive controls. In elderly patients, left ventricular mass was found to be correlated with 24-hour ambulatory blood pressure \( r = 0.47, p < 0.01 \) and 24-hour ambulatory blood pressure variability \( r = 0.52, p < 0.01 \), while ventricular arrhythmias were correlated with left ventricular mass \( r = 0.52, p < 0.01 \), the Doppler synthetic index of diastolic function E/A ratio \( r = -0.56, p < 0.01 \) and both 24-hour systolic \( r = 0.54, p < 0.01 \) and diastolic \( r = 0.59, p < 0.01 \) ambulatory blood-pressure variabilities.

These data suggest that hypertension induces in elderly patients an impairment of cardiac structure and function comparable with that already shown in younger hypertensives. Therefore, the assessment of hypertensive target-organ damage currently employed in younger subjects should be also considered in elderly hypertensives, at least when no other relevant medical disease is present.

Introduction
Hypertension has long been recognized as a major risk factor for both cerebrovascular and cardiovascular diseases in elderly subjects [1, 2]. As treatment of hypertension in the elderly is known to be effective in reducing both morbidity and mortality [3], there is growing agreement that elderly hypertensives should have a diagnostic and clinical approach similar to that currently deployed for younger subjects [4].

Several studies have shown that left ventricular mass (LVM), as determined by echocardiography, is a strong and independent predictor of subsequent cardiovascular morbidity in hypertension [5, 6]. Moreover, hypertensive subjects with an increased LVM have an impaired left ventricular filling pattern [7] and more frequent and complex ventricular arrhythmias [8–10]. Increased ventricular ectopic activity, related to both hypertension and left ventricular hypertrophy, has been also noted in elderly hypertensives [11, 12].

The recent availability of ambulatory blood pressure (ABP) monitoring in clinical practice has provided opportunities for improved assessment of blood pressure (BP) levels and hypertensive target-organ damage [13, 14].

This study was designed to investigate BP load variations and the incidence of cardiac arrhythmias, as assessed by simultaneous ambulatory BP and electrocardiographic monitoring, in a group of elderly hypertensive subjects. The relationships between ABP and cardiac arrhythmias on the one hand and LVM and filling pattern on the other were also considered.

Patients and Methods
The study sample comprised 25 consecutive elderly hypertensive men, aged 69–82 [mean age 74 (SD 4) years], referred to the hospital-based hypertension clinic of our Institution by their general practitioners after the chance finding of abnormal blood pressure values during a routine medical examination.
A control group of 25 apparently healthy elderly normotensive men, aged 67–80 [mean age 72 (8) years], was recruited among the subjects attending a municipal recreational centre (City of Rome, circoscrizione XIX). Hypertensive subjects were selected and included in the study if they showed a BP exceeding 160/95 mmHg, as measured by a conventional mercury sphygmomanometer, in three consecutive outpatient visits in a 2-month period.

No included subject had clinical, electrocardiographic or echocardiographic evidence of previous myocardial infarction, valvular or primary myocardial disease or congestive heart failure. Diabetes mellitus, renal insufficiency, or clinically significant liver disease were also excluded by conventional laboratory examinations.

None of the subjects was receiving pharmacological treatment or had ever received any kind of cardiovascular drug or antihypertensive medication. All hypertensive subjects underwent routine laboratory examination to exclude causes of secondary hypertension.

Resting 12-lead electrocardiograms were recorded from all included subjects by an Ote-Biomedica C4 unit. Left ventricular hypertrophy was defined as being present when the sum of the amplitudes of the S wave in lead VI and the R wave in lead V5 or V6 was ≥3.5 mV [15]. All electrocardiograms were interpreted by an experienced physician 'blinded' to the blood pressure status of the study patients.

Doppler-echocardiographic studies were carried out in all cases after the preliminary work-up, using a Hewlett-Packard ultrasound unit (model 77020 A). All examinations were performed and blindly interpreted by an experienced physician, whose intra-observer reproducibility (97.4%) had been previously tested over 375 consecutive echocardiographic studies. Standard M-mode echocardiograms were recorded in all subjects and parasternal long- and short-axis B-mode imaging was performed to provide reference points for M-mode examination. M-mode measurements of the left ventricle, including left ventricular systolic and diastolic diameter, left ventricular posterior wall thickness and interventricular septum thickness, were made in accordance with American Society of Echocardiography recommendations [16] over three consecutive cardiac cycles and averaged. Echocardiographic LVM was then calculated using the 'ASE-cube' formula [17], and subsequently divided by body surface area to obtain the LVM index.

Additionally, left ventricular percentage fractional shortening was calculated as a synthetic index of left ventricular systolic function [18].

Transmitral blood flow velocities were recorded by pulsed wave Doppler with the same instrument used for imaging. From an apical four-chamber view a sample volume was placed in the inflow area of the left ventricle at the level of the mitral valve tips, and the position along the line was adjusted until the highest diastolic flow velocity was recorded [19].

Particular care was taken to attain the smallest possible angle between the presumed direction of blood flow and the ultrasound beam. The following synthetic indexes of diastolic function were calculated by recorded Doppler waveforms [19]: peak early diastolic flow velocity (E peak), peak late diastolic flow velocity (A peak) and ratio between early and late peak of flow velocity (E/A ratio). All Doppler indices were calculated by averaging at least three consecutive cardiac cycles.

Simultaneous ABP and electrocardiographic monitorings were performed over 24 hours in all subjects, starting just after echocardiographic examination. The BP was measured every 15 minutes during the day (from 06 h 00 to 24 h 00) and every 30 minutes during the night (from 24 h 00 to 06 h 00) by means of a Spacelabs 5200 monitoring unit, while electrocardiographic tracings were simultaneously recorded by a Siemens Siretape 824 double-channel recorder. The following indices were derived from the ABP monitoring [14]: mean 24-hour systolic and diastolic BP, mean night-time systolic and diastolic BP and mean daytime systolic and diastolic BP. The standard deviations (SD) of all these indices were computed [20].

Electrocardiographic recordings were initially scanned at high speed and subsequently reviewed for more precise analysis by two observers, with the total number of ventricular ectopic beats being determined for each subject.

All data are expressed as mean and SD and analysed by unpaired Student's t test and Fisher and Yates' correlation coefficients. Correlation analysis was performed separately for hypertensive patients and normotensive controls.

**Results**

The two study groups were similar in age, sex and Body Mass Index (Table I).

**Electrocardiographic findings:** The prevalence of echocardiographic left ventricular hypertrophy was 28% in elderly hypertensives (7/25) and 4% in normotensive controls (1/25) (p < 0.001). Secondary repolarization abnormalities (electrocardiographic left ventricular strain pattern) [21] were absent in all subjects.

No significant correlation was shown between electrocardiographic findings (voltage amplitude) and any index deriving from Doppler-echocardiographic examination or simultaneous ABP and ECG monitorings in the study population.

**Doppler-echocardiographic findings:** No subject had reduced systolic function, assessed by fractional shortening on echocardiographic examination (Table I).

**Simultaneous ABP and ECG monitorings:** Hypertensive subjects showed significantly more ventricular ectopic beats than normotensive controls (Table II).

| Table I. General and Doppler-echocardiographic features in the study groups |
|-----------------------------|-----------------------------|-----------------------------|
| Hypertensive subjects | Normotensive subjects |
| Mean (SD) | Mean (SD) |
| **Age in years** | 74 (4) | 72 (8) |
| **Body Mass Index (kg/m²)** | 23.7 (2.8) | 23.2 (4.6) |
| **LVM index (g/m²)** | 156.2 (19.5) | 113.6 (14.8) |
| **Percentage FS** | 41.3 (2.7) | 42.4 (3.2) |
| **E peak (cm/s)** | 58.4 (12.3) | 72.3 (15.1) |
| **A peak (cm/s)** | 78.3 (13.4) | 53.5 (17.2) |
| **E/A ratio** | 0.75 (0.4) | 1.35 (0.05) |

LVM = left ventricular mass; FS = fractional shortening.

* p < 0.001.
Significant positive correlations were found between the number of ventricular ectopic beats and 24-hour systolic BP variability (r = 0.54, p < 0.01). No other significant correlation could be shown between the number of ventricular ectopic beats and the E/A ratio (r = —0.56, p < 0.01) in hypertensive subjects. A significant positive correlation was found between the number of ventricular ectopic beats and the LVM index (r = 0.52, p < 0.01) in hypertensive subjects. A significant negative correlation was found between the number of ventricular ectopic beats and the E/A ratio (r = 0.53, p < 0.01) in hypertensive subjects.

All indices deriving from ABP monitoring were found to be significantly higher in elderly hypertensives than in normotensive controls, except for night-time systolic and diastolic BP variability (Table II).

Table II. Ambulatory blood pressure and ventricular arrhythmias in the study groups

<table>
<thead>
<tr>
<th></th>
<th>Hypertensive subjects</th>
<th>Normotensive subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>24-hour SBP (mmHg)</td>
<td>152.2 (7.3)</td>
<td>129.5 (6.2)*</td>
</tr>
<tr>
<td>24-hour DBP (mmHg)</td>
<td>95.3 (10.4)</td>
<td>76.2 (6.8)*</td>
</tr>
<tr>
<td>Daytime SBP (mmHg)</td>
<td>160.4 (11.3)</td>
<td>140.3 (7.2)*</td>
</tr>
<tr>
<td>Daytime DBP (mmHg)</td>
<td>97.6 (7.4)*</td>
<td>81.2 (4.6)*</td>
</tr>
<tr>
<td>Night-time SBP (mmHg)</td>
<td>138.9 (8.1)</td>
<td>118.4 (7.8)*</td>
</tr>
<tr>
<td>Night-time DBP (mmHg)</td>
<td>77.8 (7.1)</td>
<td>62.3 (8.1)*</td>
</tr>
<tr>
<td>24-hour SBP SD (mmHg)</td>
<td>18.3 (3.2)</td>
<td>14.1 (2.4)*</td>
</tr>
<tr>
<td>24-hour DBP SD (mmHg)</td>
<td>12.8 (7.2)</td>
<td>7.6 (5.7)*</td>
</tr>
<tr>
<td>Daytime SBP SD (mmHg)</td>
<td>21.4 (4.5)</td>
<td>16.6 (5.3)*</td>
</tr>
<tr>
<td>Daytime DBP SD (mmHg)</td>
<td>11.4 (2.5)</td>
<td>8.7 (2.4)*</td>
</tr>
<tr>
<td>Night-time SBP SD (mmHg)</td>
<td>12.3 (3.2)</td>
<td>11.6 (2.5)</td>
</tr>
<tr>
<td>Night-time DBP SD (mmHg)</td>
<td>5.3 (3.1)</td>
<td>6.1 (2.7)</td>
</tr>
<tr>
<td>VEB/24 hours</td>
<td>141.8 (38.5)</td>
<td>83.7 (23.1)*</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; DBP = diastolic blood pressure; VEB = ventricular ectopic beats.

* p < 0.001.

Discussion

Left ventricular hypertrophy is a common sequela of established arterial hypertension, and has been associated with significant impairment of diastolic function and with increased ventricular ectopic activity [22]. Moreover, both electrocardiographic [23] and echocardiographic [5, 6] evidence of left ventricular hypertrophy represent strong and independent predictors of subsequent cardiovascular morbidity and even if most of the data concerning the prognostic relevance of an abnormal increase in LVM have been collected in middle-aged subjects with essential hypertension, electrocardiographic and echocardiographic left ventricular hypertrophy seem to retain a similar clinical and prognostic significance in elderly hypertensives [24].

The elderly hypertensive patients included in this study showed an increased echocardiographic LVM together with impairment of diastolic filling pattern, when compared with age-matched normotensive controls. These structural and functional cardiac abnormalities were associated with an increased frequency of rhythm disturbances, as recently observed in younger hypertensives [25]. An electrocardiographic pattern of left ventricular hypertrophy was found to be present in a sizeable percentage of our elderly hypertensive patients.

Even when clinical evidence of cardiac disease is lacking, elderly subjects may show higher values of LVM, left ventricular filling abnormalities [7] and frequent ventricular arrhythmias [26]. However, the significant differences observed in this study between elderly hypertensives and age-matched normotensive controls support a role of hypertension in inducing specific cardiac damage, at least partially independently from ageing processes. Moreover, in accordance with previous reports [27], LVM was positively correlated in our study with both 24-hour systolic BP and 24-hour systolic BP variability, expressing a possible dependence of cardiac structure on BP load even in older hypertensives.

All the data collected in this study contribute to defining target-organ involvement in elderly hypertensives which seems to be similar to that repeatedly shown in young hypertensives [24]. Left ventricular hypertrophy and ventricular arrhythmias, which represent a sensitive marker of cardiac damage in middle-aged hypertensives [8-10], should be considered in elderly hypertensive subjects, as they may herald new unfavourable events [28].

One more unanswered question in clinical practice is whether full target-organ status assessment should be offered to elderly hypertensive subjects [29]. Our study supports the idea that a staging work-up, including echocardiography, could be clinically useful in elderly hypertensives without concomitant medical diseases.
However, the cost-effectiveness of such a comprehensive approach for hypertensive elderly patients is still unknown, as the elderly population is heterogeneous and many subjects are afflicted by several medical conditions. As for most studies [29], it is difficult to regard our outpatients as representative of the whole elderly population. Further prognostic studies are needed to define the cost-effective sequence of non-invasive methods to be deployed for elderly patients with arterial hypertension.

References

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