Systolic and Diastolic Hypertension: No Relationship With Lipid and Inflammatory Markers in Haute-Garonne, France

Pedro Marques-Vidal, Jean-Pierre Cambou, Vanina Bongard, Jean-Bernard Ruidavets, and Jean Ferrières

Background: Isolated systolic hypertension (ISH) is a major cardiovascular risk factor. The prevalence of ISH, isolated diastolic (IDH), and mixed hypertension (MH) and their association with lipid, inflammatory, and endothelial cell markers were assessed.

Methods: A population sample from Haute-Garonne, France, was chosen.

Results: Prevalence of ISH, IDH, and MH was 16%, 5%, and 16%, respectively, in men, and 13%, 2%, and 9% in women. No difference was found between ISH, IDH, or MH subjects in comparison to normotensive individuals for all biologic markers studied.

Conclusions: Isolated systolic hypertension and MH are relatively common in Haute-Garonne and are not associated with lipid, inflammatory, or endothelial cell markers. Am J Hypertens 2003;16:681–684 © 2003 American Journal of Hypertension, Ltd.

Key Words: Isolated systolic hypertension, diastolic hypertension, mixed hypertension, inflammation, lipids, endothelial cells.

Although high blood pressure (BP) is an important cardiovascular risk factor, there is growing evidence that an increase in systolic BP is more deleterious than an increase in diastolic BP. Isolated systolic hypertension (ISH) is currently considered as a major risk factor for stroke in elderly subjects, and effectively treating subjects with ISH leads to a decrease in the incidence of cardiovascular events. Isolated systolic hypertension has also been shown to be related to several abnormalities in plasma prothrombotic factors and markers of endothelial dysfunction. On the basis of those findings, several guidelines have been issued calling for an increased effort directed at the control of increased systolic BP.

The prevalence of the different types of hypertension—ISH, isolated diastolic hypertension (IDH) and mixed hypertension (MH)—has been relatively well studied in several countries. Conversely, little is known regarding their prevalence in France, a country characterized by a low rate of coronary heart disease. Thus, we used the data from the last MONICA population survey conducted in Haute-Garonne, southwestern France, to assess the prevalence of ISH, IDH, and MH and their relationships with lipid, lipoprotein, inflammatory, and endothelial cell activation markers.

Methods
Study Population

The World Health Organization–MONICA Project is a study that monitors deaths due to coronary heart disease, myocardial infarction, coronary care, and risk factors in men and women aged 35 to 64 years. In Haute-Garonne, the survey was conducted on both genders. The informed consent to participate in the study was obtained from the subjects before the survey, and the overall study was approved by the Ethics Committee (Comité Consultatif pour la Protection des Personnes participant à des Recherches Biomédicales). Participation rates were 67% and 59% for men and women, respectively.

Data Collection

Subjects were advised to refrain from physical exercise, smoking, eating or drinking anything other than water for at least 10 h before the screening visit. Screening included...
BP Measurement

Systolic BP and diastolic BP were measured twice on the right arm of subjects who had been resting for at least 5 min in a comfortable position. Two consecutive measurements of systolic BP and diastolic BP were recorded to the nearest 2 mm Hg, and the mean values were used for the present analysis. Hypertension was defined as systolic BP ≥140 mm Hg, diastolic BP ≥90 mm Hg, or presence of antihypertensive treatment. Isolated systolic hypertension was defined as systolic BP ≥140 mm Hg and diastolic BP <90 mm Hg; IDH was defined as systolic BP <140 mm Hg and diastolic BP ≥90 mm Hg; and MH as systolic BP ≥140 mm Hg and diastolic BP ≥90 mm Hg. Because no information regarding pretreatment hypertensive status could be obtained for treated, controlled hypertensive subjects, the prevalence of ISH, IDH, and MH was assessed only among untreated and uncontrolled subjects. The BP reductions needed to reach target treatment goals were computed for the three hypertension groups as described previously.

Biologic Measurements

Lipids were measured on plasma EDTA samples using automated enzymatic assays (Boehringer, Mannheim, Germany). Apolipoproteins A-I and B were measured by immunoturbidimetry in an automated analyzer (Cobas-Mira, Roche Diagnostics, Germany). Fibrinogen was assessed by the method of Clauss using an automated device (Diagnostica Stago, Asnières, France). The von Willebrand factor (vWF) activity levels were assessed using a platelet aggregation technique on a BCT device (Dade Behring Marburg GmbH, Marburg, Germany). The C-reactive protein (CRP) levels were assessed by immunephelometric method (Dade Behring Marburg GmbH). Levels of soluble vascular cell adhesion molecule-1 (VCAM-1) and soluble intercellular adhesion molecule (ICAM) were assessed by immunoenzymatic methods (Immunotech, Marseilles, France). Between-series coefficients of variation were vWF, 8%; CRP, 4.4%; soluble VCAM-1, 8.7%; and soluble ICAM, 6.9%.

Statistical Analysis

Statistical analysis was conducted using SAS (SAS Institute, Cary, NC). Quantitative data were expressed as mean ± standard deviation or as adjusted mean ± standard error; qualitative data were expressed as number of subjects and percentage. Bivariate comparisons were performed using χ² or Student t test; multivariate adjustment was performed using a generalized linear model (Proc GLM of SAS). Extrapolation to the overall population aged 35 to 64 years from Haute-Garonne was performed using the estimated population data for 1996, obtained from the National Institute for Statistics and Economical Studies. Significance was established at P < .05.

Results

Clinical Characteristics

Overall, 1181 subjects were screened: 614 men and 567 women. Among them, 223 men and 137 women presented with untreated or uncontrolled hypertension, and prevalence of ISH, IDH, and MH was assessed only among those subjects. Isolated systolic hypertension was the most frequent form of hypertension in both genders, and its frequency increased with age, whereas IDH decreased and MH remained relatively stable (Mantel-Haenszel test adjusting for sex = 25.01, P < .001). In the total sample, the frequency of ISH, IDH, and MH was 16%, 5%, and 16% in men, and 13%, 2%, and 9% in women, respectively. After standardizing for the population of Haute-Garonne, the prevalence of ISH, IDH, and MH in men was 14.5%, 4.6%, and 14.0%, respectively, and 11.2%, 2.2% and 8.2%, respectively, in women.

Relationship of ISH, IDH and MH With Cardiovascular Risk Factors

In both genders, subjects with ISH, IDH, or MH were older and had higher body mass index (BMI) and triglyceride levels than normotensive subjects, whereas no difference was found for total and HDL cholesterol, apolipoprotein A-I, fibrinogen, vWF, CRP, soluble ICAM, and soluble VCAM-1 (Table 1). Women with ISH, IDH, or MH also had higher levels of apolipoprotein B (not shown), and similar findings were obtained when subjects on antihypertensive treatment were excluded from the analysis (data not shown).

Comparisons between the ISH, IDH, and MH groups showed that after adjusting for age, men with ISH had a lower mean BMI than those presenting with IDH or MH (Table 1). Conversely, no difference in BMI was found in women (data not shown). Subjects with MH had higher mean systolic BP and diastolic BP levels than subjects with ISH and IDH (Table 1). Also, in both genders, after adjusting for age and antihypertensive drug treatment, pulse pressure decreased from ISH to IDH: in men, 68 ± 1 mm Hg, 60 ± 1 mm Hg, and 43 ± 2 mm Hg (adjusted mean ± standard error) for ISH, MH, and IDH, respectively (P < .001); in women, the corresponding values were 70 ± 1 mm Hg, 66 ± 1 mm Hg, and 46 ± 4 mm Hg (P < .001). Further adjustment on smoking, alcohol drinking, BMI, educational level, and physical activity did not change the results (data not shown). No relationship was found between pulse pressure and lipid levels (total and HDL cholesterol, triglycerides, apolipoproteins A-I and B), inflammatory markers (fibrinogen and CRP), and endothelial cell activation markers (vWF, soluble ICAM and soluble VCAM-1) (Table 1). Conversely, a significant positive relationship was found between pulse pressure
Table 1. Clinical characteristics, blood pressure levels, lipid and lipoprotein levels according to type of hypertension in men

<table>
<thead>
<tr>
<th></th>
<th>Normal (n = 374)</th>
<th>ISH (n = 98)</th>
<th>IDH (n = 28)</th>
<th>MH (n = 97)</th>
<th>p1</th>
<th>p2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>47.4 ± 8.2</td>
<td>53.2 ± 9.0</td>
<td>50.0 ± 6.4</td>
<td>54.1 ± 6.1</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.5 ± 0.2</td>
<td>26.6 ± 0.4</td>
<td>28.1 ± 0.8</td>
<td>28.3 ± 0.4</td>
<td>0.001</td>
<td>0.01</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>125.7 ± 0.5</td>
<td>149.3 ± 1.2</td>
<td>134.2 ± 2.2</td>
<td>156.8 ± 1.2</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>77.6 ± 0.3</td>
<td>82.6 ± 0.6</td>
<td>92.5 ± 1.2</td>
<td>97.6 ± 0.6</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>SBP required reduction</td>
<td>−9.3</td>
<td></td>
<td>−2.5</td>
<td>−16.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP required reduction</td>
<td>−0.3</td>
<td></td>
<td>−2.5</td>
<td>−7.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.92 ± 0.7</td>
<td>5.93 ± 0.11</td>
<td>5.85 ± 0.19</td>
<td>6.07 ± 0.11</td>
<td>0.68</td>
<td>0.46</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.30 ± 0.02</td>
<td>1.27 ± 0.04</td>
<td>1.22 ± 0.07</td>
<td>1.27 ± 0.04</td>
<td>0.45</td>
<td>0.72</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.24 ± 0.06</td>
<td>1.34 ± 0.11</td>
<td>1.52 ± 0.18</td>
<td>1.63 ± 0.11</td>
<td>0.001</td>
<td>0.03</td>
</tr>
<tr>
<td>Apolipoprotein A-I (gr/L)</td>
<td>1.56 ± 0.02</td>
<td>1.56 ± 0.03</td>
<td>1.56 ± 0.05</td>
<td>1.58 ± 0.03</td>
<td>0.93</td>
<td>0.86</td>
</tr>
<tr>
<td>Apolipoprotein B (gr/L)</td>
<td>1.27 ± 0.02</td>
<td>1.31 ± 0.03</td>
<td>1.25 ± 0.05</td>
<td>1.35 ± 0.03</td>
<td>0.10</td>
<td>0.40</td>
</tr>
<tr>
<td>Fibrinogen (gr/L)</td>
<td>2.75 ± 0.03</td>
<td>2.87 ± 0.06</td>
<td>2.72 ± 0.11</td>
<td>2.82 ± 0.06</td>
<td>0.25</td>
<td>0.46</td>
</tr>
<tr>
<td>von Willebrand factor (%)</td>
<td>115 ± 2</td>
<td>115 ± 5</td>
<td>101 ± 9</td>
<td>109 ± 5</td>
<td>0.39</td>
<td>0.39</td>
</tr>
<tr>
<td>CRP (ng/mL)</td>
<td>1.58 ± 0.14</td>
<td>1.82 ± 0.27</td>
<td>1.40 ± 0.49</td>
<td>1.88 ± 0.27</td>
<td>0.68</td>
<td>0.62</td>
</tr>
<tr>
<td>sICAM (ng/mL)</td>
<td>266 ± 5</td>
<td>283 ± 10</td>
<td>269 ± 18</td>
<td>264 ± 10</td>
<td>0.42</td>
<td>0.37</td>
</tr>
<tr>
<td>sVCAM-1 (ng/mL)</td>
<td>670 ± 15</td>
<td>698 ± 28</td>
<td>735 ± 52</td>
<td>696 ± 29</td>
<td>0.54</td>
<td>0.92</td>
</tr>
</tbody>
</table>

ISH = isolated systolic hypertension; IDH = isolated diastolic hypertension; MH = mixed hypertension; SBP = systolic blood pressure; DBP = diastolic blood pressure; CRP = C-reactive protein; sICAM = soluble intercellular adhesion molecule; sVCAM-1 = soluble vascular cell adhesion molecule-1.

Results are expressed as mean ± SD (for age) or as adjusted mean ± standard error. Statistical analysis by ANOVA (for age) and by general linear models adjusting for age (for all other variables) and hypolipidemic drug treatment (for lipid and lipoprotein levels).

Column p1 stands for the four-group comparison; column p2 represents the comparison between hypertension groups.

and CRP levels (Spearman $r = 0.14$, $P = .04$ in men and $r = 0.24$, $P < .01$ in women).

Comparisons between the ISH, IDH, and MH groups showed that after adjusting for age and presence of hypolipidemic drug treatment, no difference was found regarding most lipid and lipoprotein variables (Table 1). Also, after adjusting for age, no difference was found regarding inflammatory and endothelial cell activation parameters (Table 1). Further adjustment on BMI, smoking, educational level, alcohol consumption, and physical activity (and contraceptive use and menopausal status for women) led to no significant difference between ISH, IDH, and MH for all lipid and lipoprotein variables studied (data not shown).

Discussion

There is little information regarding the prevalence of ISH in France. Our data indicate that ISH is relatively common in the population of Haute-Garonne aged 35 to 64 years, and that its frequency increases with age. Those findings are in agreement with other studies,4,5,6 and stress the need for a better screening and management of elevated BP levels among elderly subjects.

Contrary to other investigators,7 MH was relatively common in our sample. Those differences might partly be due to the fact that, in the United States, emphasis was initially put in controlling high diastolic BP levels, which might have led to a decrease in MH prevalence relative to ISH.11 Still, comparison of our data with that from other countries is hampered by different classification of the types of hypertension, the age groups studied, or by use of different thresholds. Those difficulties stress the need for a precise definition of the different types of hypertension to facilitate between-country comparisons.

In both genders, subjects with MH required significantly greater reductions of systolic BP and diastolic BP levels than subjects with ISH or IDH, which is in agreement with the literature.7 Although the small number of subjects did not allow us to perform adequate comparisons between untreated and inadequately treated subjects, our results indicate that a particular emphasis should be put on MH subjects to reach adequate BP levels.

Fibrinogen is simultaneously a coagulation factor, a hemorrheologic factor, and an inflammatory marker, which explains most of its relations with cardiovascular events.12 In this study, no difference was found between ISH, IDH, or MH and normotensive subjects regarding fibrinogen levels, although subjects with ISH and MH tended to present with higher levels of fibrinogen. It is possible that the absence of a relationship might be due to other confounding factors that were unaccounted for in the multivariate analysis. Another possible explanation might be the relatively low BP level among hypertensive subjects, which might have lessened the differences in fibrinogen levels among hypertensive relative to normotensive subjects. Still, no difference was found for CRP levels, another marker of inflammation, thus confirming the pre-
vious findings on fibrinogen. Subjects with ISH and MH tended to present with higher CRP levels than subjects with IDH (Table 1) and also had higher pulse pressure levels. Because a positive relationship was found between pulse pressure and CRP levels, our findings suggest that the association between pulse pressure and increased cardiovascular risk might be partly due to an increase in inflammatory markers.

The vWF is synthesized by the endothelial cells and its increased plasma level is considered as a marker for endothelial lesion. The vWF has also been shown to be increased among ISH and MH subjects. Still, our data showed that, at least in Haute-Garonne, there is no such increase in vWF among ISH or MH subjects relative to normotensives. Those findings were further confirmed by the lack of difference between ISH, IDH, and MH relative to normotensives regarding soluble ICAM and soluble VCAM-1, two other markers of endothelial cell activation. Overall, our data indicate that ISH, IDH, or MH is not associated with an increased endothelial cell activity in the general population of Haute-Garonne. Nevertheless, further studies are needed to better assess this point.

No significant difference was found between ISH, IDH, and MH regarding lipid and lipoprotein markers, and no correlation was found between BP and serum lipids in all hypertension groups. Thus, our data suggest that the increased arterial stiffness observed in ISH is probably not due to increased serum lipids, at least not in Haute-Garonne.

Several remarks should be made regarding this study. First, BP measurement was performed only on one occasion, and it has been shown that subjects with ISH tend to present lower systolic BP levels when ambulatory monitoring is performed. Second, undertreatment of ISH is relatively common and, therefore, it is likely that the frequency of ISH in our sample might have been overestimated. Finally, as no reliable pretreatment data regarding BP levels could be obtained from controlled hypertensive subjects, the prevalence of ISH, IDH, and MH could only be derived from untreated or inadequately treated hypertensive subjects, a method that has been used by most researchers.

In summary, our results indicate that the prevalence of ISH and MH is relatively common in middle-aged subjects from Haute-Garonne, that MH subjects have higher BP levels than ISH or IDH subjects, and that ISH is not associated with significant changes in lipid, lipoprotein, inflammatory, or endothelial cell activation markers compared to other groups of hypertension.

Acknowledgments
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References