Relationship of Office, Home, and Ambulatory Blood Pressure to Blood Glucose and Lipid Variables in the PAMELA Population

Giuseppe Mancia, Rita Facchetti, Michele Bombelli, Hernan Polo Friz, Guido Grassi, Cristina Giannattasio, Roberto Sega

Abstract—Alterations in blood glucose and cholesterol are more frequently detectable in hypertensive than in normotensive conditions. However, no information exists as to whether this phenomenon involves only office or also home and 24-hour ambulatory blood pressure (ie, when values are representative of daily life). In 2045 subjects enrolled in the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study, we measured home, 24-hour, and office blood pressure. Measurements also included fasting blood glucose and serum total and HDL cholesterol values. Prevalence of diabetes (≥126 mg/dL or use of antidiabetic drugs), impaired fasting blood glucose (≥110 to <126 mg/dL), and hypercholesterolemia (serum total cholesterol ≥240 mg/dL or 200 mg/dL) increased progressively from “optimal” to “high-normal,” “high-normal,” and “elevated” office systolic or diastolic blood pressure. Fasting blood glucose and total serum cholesterol also increased progressively from the first to the fourth group, with HDL cholesterol values showing a concomitant progressive decrease. This was also the case for quartiles of office, home, and 24-hour blood pressure. In the whole population, there was a positive correlation between serum cholesterol or blood glucose and all blood pressure values (P always <0.0001), with a much smaller and less consistent relationship with heart rate. In a multivariate analysis that included gender, body mass index, age, and antihypertensive treatment, all blood pressure values remained highly significantly related to values of either metabolic variables. Thus, in the PAMELA population, glucose and lipid values are independently related to blood pressure. This is also the case when daily life blood pressure values are considered. (Hypertension. 2005;45:1072-1077.)

Key Words: blood pressure monitoring, ambulatory ■ cholesterol ■ glucose ■ lipids

Several studies have shown that hypertensive individuals more frequently display alterations in glucose and lipid metabolism than normotensive ones.1–11 Evidence has also been obtained that alterations in lipid and glucose metabolism are more frequent in individuals with blood pressure values in the high-normal range (ie, between 130 and 139 mm Hg systolic or 85 and 89 mm Hg diastolic) than in those with lower values,1,5,7,12 suggesting that the relationship between blood pressure and metabolic alterations may have a continuous rather than a threshold-related nature.

We thought that the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study13 could provide relevant information on this issue because: (1) blood pressure, total serum cholesterol, and blood glucose were assessed in a sample representative of the general population; and (2) blood pressure measurements were obtained not only in the office but at home and during the 24 hours (ie, under conditions devoid of biological artifacts such as the white coat effect and representative of daily life values).14–15

Methods
The methodology used in the PAMELA study has been reported in detail previously.15 Briefly, 3200 individuals were selected randomly from the residents of Monza (a town in the northeast part of the Milan province) to be representative of the town population for gender, age decades (25 to 74 years), and socioeconomic characteristics, according to the criteria used in the World Health Organization Monitoring Diseases (WHO-MONICA) project conducted in the same geographic area.16–17 The overall participation rate was 64% consistently in each age–gender stratum. The demographic characteristics of nonparticipants were similar to those of participants. This was also the case for cardiovascular risk factors on the basis of information collected via telephone interviews.

Entry Data
Participants were invited to come to the outpatient clinic of the local hospital (San Gerardo) in the morning of a working day (Monday through Friday) where several data were collected. Relevant to the present study are: (1) 3 sphygmomanometric blood pressure measurements with the subject in the sitting position, starting 10 minutes after the beginning of the medical visit and including heart rate measurement (palpatory method) after each blood pressure measure-
Laboratory examinations included blood pressure and heart rate measurements after removal of the ambulatory monitoring device; and (5) information on office, home, and 24-hour heart rate values. Subjects were divided into 4 quartiles according to the office blood pressure criteria of the guidelines of the European Societies of Hypertension and Cardiology.

### Data Analysis

The 6 office (3 before and 3 after ambulatory blood pressure monitoring) and 2 home blood pressure measurements were separately averaged. Ambulatory blood pressure values were edited for artifacts according to preselected criteria and averaged for the 24 hours. Averages were also calculated for the corresponding office, home, and 24-hour heart rate values. Subjects were divided into 4 groups according to the office blood pressure criteria of the guidelines of the European Societies of Hypertension and Cardiology.

### Table 1: Demographic and Clinical Characteristics (means ± SD or %) of Subjects in Different Office SBP and DBP Categories According to the European Societies of Hypertension and Cardiology Guidelines Criteria

<table>
<thead>
<tr>
<th>Variables</th>
<th>Optimal (office SBP/DBP &lt; 140/90 mm Hg)</th>
<th>Normal (office SBP/DBP 140–149/90–94 mm Hg)</th>
<th>High-Normal (office SBP/DBP 150–159/95–104 mm Hg)</th>
<th>Hypertension (office SBP/DBP ≥ 160/105 mm Hg)</th>
<th>P&lt; for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>547</td>
<td>382</td>
<td>285</td>
<td>215</td>
<td>---</td>
</tr>
<tr>
<td>Mean office SBP/DBP, mm Hg</td>
<td>119.2 ± 2/79.9 ± 2</td>
<td>121.5 ± 3/81.1 ± 3</td>
<td>130.2 ± 4/86.6 ± 4</td>
<td>151.7 ± 18/92.5 ± 18</td>
<td>---</td>
</tr>
<tr>
<td>Male prevalence, %</td>
<td>42.8</td>
<td>52.3</td>
<td>53.5</td>
<td>57.2</td>
<td>---</td>
</tr>
<tr>
<td>Age, y</td>
<td>50.5 ± 10.8</td>
<td>52.7 ± 12.2</td>
<td>52.1 ± 13.2</td>
<td>58.2 ± 11.3</td>
<td>---</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>33.9</td>
<td>31.4</td>
<td>27.1</td>
<td>21.1</td>
<td>---</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.0 ± 3.3</td>
<td>24.8 ± 3.7</td>
<td>25.7 ± 3.9</td>
<td>27.2 ± 4.7</td>
<td>---</td>
</tr>
<tr>
<td>Serum total cholesterol, mg/dL</td>
<td>207.1± 4/82.0 ± 4</td>
<td>220.5 ± 4/82.5 ± 4</td>
<td>225.7 ± 4/80.1 ± 4</td>
<td>235.1 ± 4/81.5</td>
<td>---</td>
</tr>
<tr>
<td>Serum HDL cholesterol, mg/dL</td>
<td>58.9 ± 15.2</td>
<td>55.1 ± 15.1</td>
<td>55.6 ± 16.7</td>
<td>54.0 ± 15.1</td>
<td>---</td>
</tr>
<tr>
<td>Blood glucose, mg/dL</td>
<td>82.8 ± 8.3</td>
<td>87.8 ± 8.2</td>
<td>92.7 ± 23.7</td>
<td>95.5 ± 23.3</td>
<td>---</td>
</tr>
<tr>
<td>Hypercholesterolemia, %, ≥240 mg/dL</td>
<td>19.3</td>
<td>31.5</td>
<td>35.8</td>
<td>45.0</td>
<td>---</td>
</tr>
<tr>
<td>Hypercholesterolemia, %, ≥200 mg/dL</td>
<td>53.3</td>
<td>68.7</td>
<td>73.9</td>
<td>80.7</td>
<td>---</td>
</tr>
<tr>
<td>Impaired fasting glucose, %, 110–126 mg/dL</td>
<td>0.9</td>
<td>2.2</td>
<td>3.9</td>
<td>5.1</td>
<td>---</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>0</td>
<td>2.2</td>
<td>3.3</td>
<td>5.1</td>
<td>---</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

**P<0.05 vs normal; †P<0.05 vs high-normal; ‡P<0.05 vs hypertension.**

### Table 2: Demographic and Clinical Characteristics (means ± SD or %) of Subjects in Office Systolic Blood Pressure Quartiles

<table>
<thead>
<tr>
<th>Variables</th>
<th>First (office SBP &lt; 118.0 mm Hg)</th>
<th>Second (office SBP 118.0–130.0 mm Hg)</th>
<th>Third (office SBP 130.0–146.0 mm Hg)</th>
<th>Fourth (office SBP ≥ 146.0 mm Hg)</th>
<th>P&lt; for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>478</td>
<td>530</td>
<td>519</td>
<td>518</td>
<td>---</td>
</tr>
<tr>
<td>Mean office SBP/DBP, mm Hg</td>
<td>108.7 ± 5.6/73.0 ± 6.4</td>
<td>122.8 ± 3.5/81.3 ± 6.4</td>
<td>136.1 ± 4.6/86.5 ± 7.1</td>
<td>162.3 ± 14.8/93.8 ± 9.8</td>
<td>0.05/0.05</td>
</tr>
<tr>
<td>Male prevalence, %</td>
<td>34.3</td>
<td>55.7</td>
<td>58.4</td>
<td>52.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Age, y</td>
<td>40.3 ± 10.2</td>
<td>46.2 ± 11.8</td>
<td>54.5 ± 12.3</td>
<td>62.0 ± 9.4</td>
<td>0.05</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>35.2</td>
<td>30.0</td>
<td>26.4</td>
<td>19.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.2 ± 3.3</td>
<td>25.3 ± 3.9</td>
<td>26.5 ± 4.3</td>
<td>27.3 ± 5.0</td>
<td>NS</td>
</tr>
<tr>
<td>Serum total cholesterol, mg/dL</td>
<td>206.2 ± 41.0</td>
<td>220.4 ± 41.2</td>
<td>231.4 ± 41.4</td>
<td>237.1 ± 41.4</td>
<td>0.05</td>
</tr>
<tr>
<td>Serum HDL cholesterol, mg/dL</td>
<td>58.1 ± 15.1</td>
<td>55.2 ± 16.1</td>
<td>55.0 ± 14.9</td>
<td>53.8 ± 15.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Blood glucose, mg/dL</td>
<td>83.0 ± 9.2</td>
<td>88.6 ± 18.4</td>
<td>93.8 ± 25.7</td>
<td>96.7 ± 22.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypercholesterolemia, %, ≥240 mg/dL</td>
<td>20.4</td>
<td>30.5</td>
<td>42.8</td>
<td>46.2</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypercholesterolemia, %, ≥200 mg/dL</td>
<td>50.8</td>
<td>70.3</td>
<td>78.8</td>
<td>81.9</td>
<td>0.05</td>
</tr>
<tr>
<td>Impaired fasting glucose, %, 110–126 mg/dL</td>
<td>1.1</td>
<td>2.1</td>
<td>4.2</td>
<td>6.2</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>0.2</td>
<td>2.3</td>
<td>3.3</td>
<td>7.8</td>
<td>0.05</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

*P<0.05 vs second quartile; †P<0.05 vs third quartile; ‡P<0.05 vs fourth quartile.
Table 3. Demographic and Clinical Characteristics (means±SD or %) of Subjects in Home SBP Quartiles

<table>
<thead>
<tr>
<th>Quartiles</th>
<th>First (home SBP &lt;111.0 mm Hg)</th>
<th>Second (home SBP 111.0–122.0 mm Hg)</th>
<th>Third (home SBP 122.0–135.5 mm Hg)</th>
<th>Fourth (home SBP ≥135.5 mm Hg)</th>
<th>P&lt; for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>464</td>
<td>457</td>
<td>475</td>
<td>474</td>
<td></td>
</tr>
<tr>
<td>Mean office SBP/DBP, mm Hg</td>
<td>102.5±6.3/66.9±7.2</td>
<td>116.5±3.2/73.8±6.2</td>
<td>127.9±4.7/79.4±7.9</td>
<td>150.9±12.6/85.7±10.2</td>
<td></td>
</tr>
<tr>
<td>Male prevalence, %</td>
<td>23.0*†‡</td>
<td>57.5</td>
<td>63.5</td>
<td>60.0</td>
<td>0.05</td>
</tr>
<tr>
<td>Age, y</td>
<td>42.0±10.5††</td>
<td>46.0±12.2††</td>
<td>51.7±12.3†</td>
<td>61.1±10.1‡</td>
<td>0.05</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>25.7</td>
<td>31.5</td>
<td>28.4</td>
<td>24.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.2±3.6††</td>
<td>25.2±3.9‡†</td>
<td>26.3±4.1‡</td>
<td>27.3±4.8 NS</td>
<td></td>
</tr>
<tr>
<td>Serum total cholesterol, mg/dL</td>
<td>210.1±39.4††</td>
<td>221.0±43.8††</td>
<td>230.2±42.3</td>
<td>234.4±42.2 0.05</td>
<td></td>
</tr>
<tr>
<td>Serum HDL cholesterol, mg/dL</td>
<td>60.6±15.7††</td>
<td>55.0±15.3</td>
<td>53.5±14.3</td>
<td>53.6±15.8 0.05</td>
<td></td>
</tr>
<tr>
<td>Blood glucose, mg/dL</td>
<td>83.8±10.5††</td>
<td>88.6±10.8‡†</td>
<td>93.6±28.1‡</td>
<td>97.1±26.1 0.05</td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia, %, ≥240 mg/dL</td>
<td>23.8††</td>
<td>30.6†</td>
<td>40.2</td>
<td>44.9</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypercholesterolemia, %, ≥200 mg/dL</td>
<td>58.2††</td>
<td>68.8†</td>
<td>75.7</td>
<td>80.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Impaired fasting glucose, %, 110–126 mg/dL</td>
<td>1.1‡†</td>
<td>2.4‡</td>
<td>4.4</td>
<td>5.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>0.9†‡</td>
<td>0.9†‡</td>
<td>4.0‡</td>
<td>7.6</td>
<td>0.05</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.
*P<0.05 vs second quartile; †P<0.05 vs third quartile; ‡P<0.05 vs fourth quartile.

Table 4. Demographic and Clinical Characteristics (means±SD or %) of Subjects in 24-Hour SBP Quartiles

<table>
<thead>
<tr>
<th>Quartiles</th>
<th>First (24-hour SBP &lt;111.9 mm Hg)</th>
<th>Second (24-hour SBP 111.9–118.9 mm Hg)</th>
<th>Third (24-hour SBP 118.9–126.6 mm Hg)</th>
<th>Fourth (24-hour SBP ≥126.6 mm Hg)</th>
<th>P&lt; for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>508</td>
<td>507</td>
<td>507</td>
<td>508</td>
<td></td>
</tr>
<tr>
<td>Mean office SBP/DBP, mm Hg</td>
<td>106.9±3.9/67.3±4.1</td>
<td>115.5±2.0/72.2±4.3</td>
<td>122.4±2.2/75.9±4.6</td>
<td>136.4±9.1/82.3±7.2</td>
<td></td>
</tr>
<tr>
<td>Male prevalence, %</td>
<td>29.7*†‡</td>
<td>49.3*†‡</td>
<td>58.7†‡</td>
<td>63.9</td>
<td>0.05</td>
</tr>
<tr>
<td>Age, y</td>
<td>46.1±12.5*†‡</td>
<td>48.3±13.3††</td>
<td>51.5±13.8‡</td>
<td>58.1±12.0 0.05</td>
<td></td>
</tr>
<tr>
<td>Smoking, %</td>
<td>27.4</td>
<td>25.8</td>
<td>27.2</td>
<td>28.7</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.9±3.7*††</td>
<td>25.5±4.4†</td>
<td>25.8±3.9‡</td>
<td>27.1±5.0 0.05</td>
<td></td>
</tr>
<tr>
<td>Serum total cholesterol, mg/dL</td>
<td>215.5±43.1††</td>
<td>219.5±41.9††</td>
<td>227.9±41.3</td>
<td>233.2±42.7 0.05</td>
<td></td>
</tr>
<tr>
<td>Serum HDL cholesterol, mg/dL</td>
<td>59.1±16.2*††</td>
<td>55.2±14.8</td>
<td>54.8±15.4</td>
<td>52.9±14.9 0.05</td>
<td></td>
</tr>
<tr>
<td>Blood glucose, mg/dL</td>
<td>84.5±9.7*†‡</td>
<td>89.4±17.5†</td>
<td>91.2±18.8‡</td>
<td>98.0±30.6 0.05</td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia, %, ≥240 mg/dL</td>
<td>26.1†‡</td>
<td>30.2†</td>
<td>39.7</td>
<td>44.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypercholesterolemia, %, ≥200 mg/dL</td>
<td>62.3†‡</td>
<td>67.4†</td>
<td>75.1</td>
<td>78.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Impaired fasting glucose, %, 110–126 mg/dL</td>
<td>2.2†</td>
<td>3.0</td>
<td>3.6</td>
<td>5.2</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>0.2*†‡</td>
<td>2.6‡</td>
<td>2.8‡</td>
<td>8.3</td>
<td>0.05</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.
*P<0.05 vs second quartile; †P<0.05 vs third quartile; ‡P<0.05 vs fourth quartile.
Variable | Glycemia, mg/dL | Cholesterol, mg/dL | Body Mass Index, kg/m²
--- | --- | --- | ---
Office SBP, mm Hg | 0.25* | 0.25* | 0.32*
Home SBP, mm Hg | 0.25* | 0.21* | 0.34*
24-hour SBP, mm Hg | 0.23* | 0.16* | 0.26*
Office DBP, mm Hg | 0.21* | 0.24* | 0.36*
Home DBP, mm Hg | 0.18* | 0.22* | 0.33*
24-hour DBP, mm Hg | 0.17* | 0.15* | 0.19*
Office HR, bpm | 0.13* | 0.04 | 0.02
Home HR, bpm | 0.09† | 0.08† | –0.03
24-hour HR, bpm | 0.04 | 0.01 | –0.02

*P<0.0001, †P<0.05.

No. of patients on which different measures were obtained ranged from 1831 to 2039.

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

Table 5. Person Correlation Coefficient Between Metabolic, Anthropometric, Blood Pressure, and Heart Rate Values

Table 6. Multivariate Analysis With Glycemia as the Dependent Variable

Discussion

In the PAMELA study population, the prevalence of diabetes, impaired fasting glucose, and hypercholesterolemia was greater in subjects with hypertension than in those with normotension on the basis of office blood pressure values. Furthermore, all 3 conditions became progressively more frequent from subjects with optimal to those with normal, high-normal, and elevated office blood pressure, with a concomitant progressive increase in average blood glucose and total serum cholesterol and a reduction in HDL cholesterol values.

Finally, all the above findings were replicated when subdivision into blood pressure subgroups was based on home or ambulatory rather than on office blood pressures, and all 3 pressures showed an independent and positive relationship with blood glucose and total serum cholesterol values even in a multivariate analysis that considered the contribution of other factors (ie, age, gender, body mass index, and antihypertensive treatment, as well as serum total cholesterol for blood glucose and blood glucose for total serum cholesterol). This confirms previous findings that...
alterations in glucose and lipid metabolism cluster with blood pressure alterations,\textsuperscript{1–12} making diabetes, prediabetes, and hypercholesterolemia more frequent in the presence than in the absence of a blood pressure elevation. It also provides clear-cut evidence that in the population, glucose and lipid variables are related to blood pressure in a continuous fashion, which means that their abnormalities have a different prevalence even within the normal blood pressure range, that is, diabetes, prediabetes, and hypercholesterolemia are considerably more frequent in the group with high-normal than in those with normal or optimal office blood pressures. Finally, it shows for the first time that what is observed when subjects are classified by their office blood pressure occurs also when classification is based on home and ambulatory values (ie, on values that are not just occasional but typical of daily life).

Several other findings of our study deserve to be mentioned. One, the observation that alterations in glucose and lipid metabolism are related not only to office but also to home and ambulatory blood pressure is important because in normotensive and hypertensive subjects, office blood pressure is frequently affected by the white coat effect (ie, by the pressor response induced by stimulation of the sympathetic nervous system triggered by an alerting reaction).\textsuperscript{14,20–21} Although relatively ineffective on serum cholesterol values, this stimulation may raise blood glucose in a way that favors its relationship with a blood pressure elevation.\textsuperscript{22–25} This is not the case for home and 24-hour blood pressures, which are virtually devoid of any pressor effect.\textsuperscript{26} Two, in the PAMELA study, home blood pressure was measured only twice within the same day, thereby not exploiting the full potential of these measurements, which can be spread over days and weeks. The finding that home blood pressure correlated with blood glucose and cholesterol fraction as well as ambulatory blood pressure points toward the clinical relevance of the approach. Three, in the subjects of the PAMELA population, blood glucose and total serum cholesterol values showed a positive correlation that was weaker than that for either variable displayed with office, home, or ambulatory blood pressure. Furthermore, and more important, the correlation between these 2 metabolic variables disappeared in the multivariate analysis, at variance with the correlation either of them showed with in-office and out-of-office blood pressure values, which was preserved. Four, at variance from blood pressure, blood glucose and total serum cholesterol show an inconsistent correlation with heart rate values, regardless of whether they were measured in the doctor’s office, at home, or during the 24 hours. Because heart rate is a marker of sympathetic tone,\textsuperscript{27} this may appear to score against a sympathetic hyperactivity as an important common mechanism for the blood pressure and the metabolic alterations. However, it should be considered that cardiac and peripheral sympathetic activities do not always proceed “pari passu,” which makes heart rate a “sympathetic” marker of limited sensitivity.\textsuperscript{28}

**Perspectives**

Our findings indicate that a blood pressure elevation is separately related to alterations in glucose and lipid abnormalities, possibly playing a causal role for both. We can speculate that this role is exerted trough the vasoconstriction that characterizes a chronic hypertensive state\textsuperscript{29} because this hemodynamic phenomenon may adversely affect glucose and lipid metabolism. In the skeletal muscle, vasoconstriction increases the distance insulin has to travel to facilitate glucose disposal across the cell membrane.\textsuperscript{30} In adipose and hepatic tissue, it may slow down the disposal of the various components of the lipid profile.\textsuperscript{31–33}

**References**

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