Different Impact of the Metabolic Syndrome on Left Ventricular Structure and Function in Hypertensive Men and Women

Giuseppe Schillaci, Matteo Pirro, Giacomo Pucci, Massimo R. Mannarino, Fabio Gemelli, Donatella Siepi, Gaetano Vaudo, Elmo Mannarino

Abstract—Metabolic syndrome (MS) is increasingly recognized as an important cardiovascular risk factor in hypertension, but its influence on left ventricular (LV) mass and function in the 2 genders has not been specifically addressed. Among 618 nondiabetic, untreated hypertensive subjects, echocardiographically detected LV mass was significantly greater in subjects with MS. A significant interaction was observed between sex and the MS (P<0.003 for the multiplicative interaction term). Compared with women without the MS, those with the syndrome had a 24% greater LV mass (49.5±12 versus 40.0±10 g×m⁻²; P<0.001), whereas the difference was only 9% in men (50.3±12 versus 46.1±10 g×m⁻²; P=0.003). A greater prevalence of LV hypertrophy was found in women (37% versus 14%; P<0.001) but not in men (39% versus 29%; P=0.09) with the MS. After adjustment for the effect of age, body mass index, 24-hour systolic blood pressure, and several confounders, the MS was independently associated with a greater LV mass index in women (regression coefficient, 4.80; P<0.001) but not in men. Women with the MS also had a greater LV relative wall thickness (0.42±0.07 versus 0.39±0.07; P=0.004) and a depressed afterload-corrected midwall fractional shortening (94.0±12% versus 101.0±13%; P<0.001) than women without the syndrome, whereas no differences emerged in men. We conclude that, in untreated hypertension, MS has a different impact on LV hypertrophy and function in men and women. The effect of MS is more pronounced in women and is partly independent from the effect of several hemodynamic and nonhemodynamic determinants of LV mass. (Hypertension. 2006;47:881-886.)

Key Words: hypertrophy ■ remodeling ■ metabolism ■ gender ■ risk factors

The metabolic syndrome (MS), a clustering of lipid and nonlipid cardiovascular risk factors, is increasingly recognized as an independent predictor of cardiovascular disease in hypertension.¹ The notion that the MS may have different relative importance for atherogenesis and cardiovascular disease in the 2 genders arises from observations indicating that elevated triglycerides and decreased high-density lipoprotein cholesterol, 2 basic components of the syndrome, are better predictors of the risk of adverse outcomes in women than in men.²⁴ Moreover, in those studies in which the prognostic impact of the MS has been examined separately in men and women, the coronary or cardiovascular morbidity/mortality hazard ratios associated with the syndrome were almost invariably found to be higher in the female sex.¹⁵⁻¹⁰ Similarly, Iglseder et al¹¹ have observed in a healthy population that the effect of MS on carotid intima-media thickness is more pronounced in women than in men. Left ventricular (LV) hypertrophy, a major manifestation of hypertensive heart disease, is a strong and independent herald for cardiovascular morbidity and mortality,¹²¹³ and its treatment-induced regression has been unequivocally associated with an improved cardiovascular prognosis, even after accounting for the confounding effect of treatment-induced blood pressure (BP) reduction.¹⁴¹⁵ Echocardiographic studies conducted in hypertensive subjects or in the general population have generally concluded that participants with metabolic risk factors¹⁶¹⁷ or with the MS¹⁸⁻²¹ have elevated LV mass or increased prevalence of LV hypertrophy. We hypothesized that a sex-specific effect of MS on LV hypertrophy might be one basic mechanism underlying the stronger adverse prognostic significance of the MS in women. Therefore, the aim of the present study was to investigate the impact of the MS on LV hypertrophy and function in hypertensive men and women taken separately. This question was addressed in a sample of white adult patients with essential hypertension, free from diabetes and cardiovascular disease, who had never received antihypertensive drug treatment.

Methods

We analyzed data of 748 consecutive subjects with never-treated essential hypertension, who were referred to our hypertension outpatient clinic by their general practitioners for baseline, off-
treatment evaluation. All of the subjects fulfilled the following inclusion criteria: (1) recent (<3 years) diagnosis of hypertension (office BP ≥140/90 mm Hg on ≥3 visits at a 1-week interval); and (2) no clinical or laboratory evidence of heart failure, coronary heart disease, previous stroke, valvular defects, or secondary causes of hypertension, diabetes, or important concomitant disease. The duration of hypertension was established after cross-checking the patients’ history and the records of the general practitioners. The self-reported duration of hypertension was cross-checked with the records of the general practitioners. A total of 119 patients (16%) were excluded from the study for poor-quality echocardiograms, and 11 (1%) were excluded for poor-quality 24-hour BP monitoring, thus leaving 618 patients for analysis. Subjects with suboptimal echocardiographic tracings were older (54.0±12 versus 47.8±11 years; *P*<0.01) and had higher body mass index (28.3±4 versus 27.3±4 kg/m²; *P*<0.01), but not BP (155±20/95±11 versus 153±18/95±10 mm Hg, *P* value was not significant), than subjects with technically adequate tracings. The MS was defined, according to the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, by the presence, in addition to hypertension, of ≥2 of the following criteria: (1) serum triglyceride levels ≥1.69 mmol/L (150 mg/dL), (2) serum HDL cholesterol <1.04 mmol/L (40 mg/dL) in men and <1.30 mmol/L (50 mg/dL) in women, (3) fasting plasma glucose ≥6.11 mmol/L (110 mg/dL), and (4) waist circumference >102 cm in men or >88 cm in women. All of the subjects gave informed consent to the study, which was approved by the institutional ethics committee.

Waist circumference was measured with a soft tape on standing subjects at the iliac crest, at the end of a normal expiration. Office BP was measured by a physician in the hospital outpatient clinic with a mercury sphygmomanometer, with the subject sitting for ≥10 minutes. The average of 6 measurements on ≥2 sessions was considered for the analysis. Ambulatory BP was recorded using an oscillometric device (models 90202 and 90207, SpaceLabs), set to take a reading every 15 minutes throughout the 24 hours. Fasting plasma glucose, serum total cholesterol, and triglycerides were determined by enzymatic colorimetric method. Serum high-density lipoprotein cholesterol was measured by enzymatic colorimetric method after precipitation with polyethilenglycole. Low-density lipoprotein cholesterol was calculated by means of the Friedewald formula. Plasma insulin levels, determined by ELISA (Mercodia AB), were available in 418 subjects. The intraassay and interassay coefficients of variation for insulin were 3.5% and 3.2%, respectively. Insulin sensitivity was estimated from the homeostasis model assessment ([glucose in mmol/L×insulin in μU/mL]/22.5).

**Echocardiography**

The M-mode echocardiographic study of the left ventricle was performed under 2D control, as reported previously, by 2 investigators (G.S. and F.G.) who were unaware of patients’ clinical data. LV mass was indexed by height²0.724 to correct for the effect of overweight. LV hypertrophy was defined as a LV mass index inappropriately high LV mass, was estimated on the basis of the cardiac load, a well-known physiological concept referred to as inappropriately high LV mass, was estimated on the basis of the cardiac load, a well-known physiological concept referred to as inappropriately high LV mass, was estimated on the basis of the cardiac load, a well-known physiological concept referred to as (27.8%) of 365 men. Some demographic and clinical characteristics of the study participants are reported in Table 1. Significant differences were found for age, body mass index, office and average 24-hour systolic and diastolic BP, office heart rate, duration of hypertension, smoking, alcohol intake, serum creatinine, and serum cholesterol were considered as explanatory variables in the adjusted models.

**Statistical Analysis**

SPSS statistical package (SPSS Inc) was used for all of the statistical analyses. The effects of sex and the MS on LV mass index and other cardiac parameters were assessed by general linear model analysis, first without any adjustments and then with adjustment for potential confounders. Interaction between sex and the MS was formally tested by assessing the significance of the multiplicative 2-way interaction term “sex×MS” along with the main effects of sex and the MS. The influence on LV mass index of several potentially relevant variables was identified using linear stepwise regression. Together with a dummy variable indicating the MS, age, body mass index, office and average 24-hour systolic and diastolic BP, office heart rate, duration of hypertension, smoking, alcohol intake, serum creatinine, and serum cholesterol were considered as explanatory variables in the adjusted models.

**Results**

The MS was present in 67 (26.5%) of 253 women and in 101 (27.8%) of 365 men. Some demographic and clinical characteristics of the study participants are reported in Table 1. Subjects with the MS did not differ from controls in terms of age, smoking habits, duration of hypertension, and total and low-density lipoprotein cholesterol concentration. Men with the MS had higher heart rate and 24-hour systolic BP values, whereas no significant differences in BP values were found in women. By selection, significant differences were found for the remaining components of the MS and for body mass index, as well as for fasting insulin and homeostasis model assessment-insulin resistance values.

In the whole population, a 2-factor ANOVA model revealed a significant effect of sex (F=12.831; *P*<0.001) and the MS (F=50.484; *P*<0.001) on height-adjusted LV mass (Table 2). The analysis of the interaction term “sex×MS” revealed a highly significant effect of sex on the association between the MS and LV mass index, both before (F=7.433; *P*=0.007) and after adjustment for the effect of age (F=8.283; *P*=0.004). As shown in Table 2, women with the MS had a significant 24% increase in LV mass index than women without the syndrome (49.5 versus 40.0 g/m²; *P*<0.001), whereas this difference was only 9% in men (50.3 versus 46.1 g/m²; *P*=0.002). Women, but not men, with the MS had a higher prevalence of LV hypertrophy and a more concentric geometric pattern (Table 2). In women, an inappropriately high LV mass for cardiac workload and body
size was found more often in the presence than in the absence of the MS (28% versus 5%; P<0.001), whereas no significant difference was observed in men.

In a multiple regression model (Table 3), after adjustment for the effect of age, 24-hour systolic BP, body mass index, and smoking (all P<0.05), the MS was independently associated with a greater LV mass index in women (regression coefficient, 4.80; P<0.001) but not in men. Among women, LV mass was higher in individuals with the MS both before (48.4±10 versus 37.3±8 g×m⁻²; P<0.001) and after the

TABLE 2. Echocardiographic Characteristics of Hypertensive Women and Men by Metabolic Pattern

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women (n=253)</th>
<th>Men (n=365)</th>
<th>P</th>
<th>Sex</th>
<th>MS</th>
<th>Sex/MS Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventricular septum, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No MS (n=186)</td>
<td>9.5 (1)</td>
<td>10.4 (1)</td>
<td>&lt;0.001</td>
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<td></td>
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</tr>
<tr>
<td>MS (n=67)</td>
<td>10.2 (1)</td>
<td>10.7 (2)</td>
<td>0.03</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>LV internal diameter, mm</td>
<td>46.1 (4)</td>
<td>47.5 (4)</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No MS (n=264)</td>
<td>50.3 (4)</td>
<td>51.0 (4)</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS (n=101)</td>
<td>53.8 (1.0)</td>
<td>55.5 (1.0)</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV mass index, g×m⁻²</td>
<td>40.0 (10)</td>
<td>49.5 (12)</td>
<td>&lt;0.001</td>
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<td></td>
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<tr>
<td>No MS (n=101)</td>
<td>50.3 (12)</td>
<td>53.8 (12)</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS (n=186)</td>
<td>46.1 (10)</td>
<td>50.3 (12)</td>
<td>0.003</td>
<td></td>
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<tr>
<td>LV hypertrophy, &gt;51 g×m⁻²</td>
<td>14</td>
<td>37</td>
<td>&lt;0.001</td>
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<tr>
<td>No MS (n=186)</td>
<td>29</td>
<td>39</td>
<td>0.09</td>
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<td></td>
</tr>
<tr>
<td>MS (n=365)</td>
<td>39</td>
<td>42</td>
<td>0.04</td>
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<tr>
<td>LV mass, % from predicted</td>
<td>103.6 (18)</td>
<td>122.4 (20)</td>
<td>&lt;0.001</td>
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<tr>
<td>No MS (n=186)</td>
<td>112.2 (21)</td>
<td>119.5 (26)</td>
<td>0.02</td>
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</tr>
<tr>
<td>MS (n=365)</td>
<td>119.5 (26)</td>
<td>122.4 (20)</td>
<td>0.01</td>
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<tr>
<td>Inappropriately high LV mass, %</td>
<td>5</td>
<td>28</td>
<td>&lt;0.001</td>
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</tr>
<tr>
<td>No MS (n=186)</td>
<td>16</td>
<td>26</td>
<td>0.08</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS (n=365)</td>
<td>26</td>
<td>28</td>
<td>0.12</td>
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<tr>
<td>Relative wall thickness</td>
<td>0.39 (0.07)</td>
<td>0.42 (0.07)</td>
<td>0.004</td>
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<tr>
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<td>0.41 (0.07)</td>
<td>0.42 (0.07)</td>
<td>0.20</td>
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</tr>
<tr>
<td>MS (n=365)</td>
<td>0.42 (0.07)</td>
<td>0.41 (0.07)</td>
<td>0.05</td>
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<td></td>
</tr>
<tr>
<td>Endocardial FS</td>
<td>38.9 (6)</td>
<td>37.4 (7)</td>
<td>0.09</td>
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<td></td>
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<tr>
<td>No MS (n=186)</td>
<td>37.0 (6)</td>
<td>36.8 (6)</td>
<td>0.84</td>
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<tr>
<td>Midwall FS</td>
<td>17.9 (2)</td>
<td>16.5 (2)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No MS (n=264)</td>
<td>16.5 (2)</td>
<td>16.2 (0.3)</td>
<td>0.39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS (n=101)</td>
<td>16.5 (2)</td>
<td>16.2 (0.3)</td>
<td>0.39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midwall FS, % from predicted</td>
<td>101.0 (13)</td>
<td>94.0 (12)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No MS (n=186)</td>
<td>93.5 (16)</td>
<td>92.3 (16)</td>
<td>0.52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS (n=365)</td>
<td>92.3 (16)</td>
<td>94.0 (12)</td>
<td>0.001</td>
<td></td>
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</tr>
<tr>
<td>Peak E velocity, m×s⁻¹</td>
<td>0.73 (0.18)</td>
<td>0.72 (0.18)</td>
<td>0.48</td>
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<tr>
<td>No MS (n=186)</td>
<td>0.68</td>
<td>0.67</td>
<td>0.68</td>
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</tr>
<tr>
<td>MS (n=365)</td>
<td>0.67</td>
<td>0.68</td>
<td>0.68</td>
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<td></td>
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</tr>
<tr>
<td>Peak A velocity, m×s⁻¹</td>
<td>0.70 (0.16)</td>
<td>0.74 (0.17)</td>
<td>0.09</td>
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</tr>
<tr>
<td>No MS (n=186)</td>
<td>0.62</td>
<td>0.65</td>
<td>0.17</td>
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<td></td>
</tr>
<tr>
<td>MS (n=365)</td>
<td>0.65</td>
<td>0.67</td>
<td>0.17</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>E/A velocity ratio</td>
<td>1.10 (0.38)</td>
<td>1.01 (0.32)</td>
<td>0.052</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No MS (n=186)</td>
<td>1.14 (0.36)</td>
<td>1.08 (0.25)</td>
<td>0.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS (n=365)</td>
<td>1.08 (0.25)</td>
<td>1.14 (0.36)</td>
<td>0.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted E/A velocity ratio</td>
<td>1.12 (0.32)</td>
<td>1.04 (0.29)</td>
<td>0.064</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No MS (n=186)</td>
<td>1.04 (0.28)</td>
<td>1.06 (0.30)</td>
<td>0.56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS (n=365)</td>
<td>1.06 (0.30)</td>
<td>1.04 (0.28)</td>
<td>0.56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV isovolumic relaxation time, ms</td>
<td>93 (19)</td>
<td>98 (19)</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No MS (n=186)</td>
<td>95 (18)</td>
<td>96 (18)</td>
<td>0.58</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS (n=365)</td>
<td>96 (18)</td>
<td>95 (18)</td>
<td>0.58</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P values of the main and interaction effects are reported. Values are mean (SD) or percentages. E/A velocity ratio is normalized for an age of 50 years and a heart rate of 75 beats/min.
menopause (50.8±10 versus 42.9±10 g m⁻², P=0.001). In either group, these differences held in fully adjusted regression models, which included all of the above variables (adjusted LV mass 44.1 versus 38.7 g m⁻², P=0.006, and 49.6 versus 43.7 g m⁻², P=0.022, respectively).

The analysis of the relationship between the single components of the MS and LV structure (Table 4) showed that, in women, low high-density lipoprotein cholesterol and high triglyceride concentration were independently associated with a higher LV mass index after taking into account the effects of age, body mass index, average 24-h systolic BP, smoking, and alcohol intake. Additional adjustment for the confounding effect of waist circumference weakened the relation of LV mass to high triglycerides (P=0.087), whereas the relation with HDL cholesterol remained significant (P=0.021). In contrast, none of these associations were significant in men.

LV chamber systolic function, assessed through endocardial FS, was slightly and nonsignificantly reduced in women with the MS (Table 2). However, significant differences appeared when midwall FS, a more physiological measure of myocardial function, was considered. Women with the MS had depressed afterload-corrected midwall FS compared with women without the syndrome (94.0±12% versus 101.0±13%; P<0.001), whereas no difference emerged in men (92.3±16% versus 93.5±16%; P=0.52). In the whole population, sex significantly modified the relation between the MS and midwall FS (women=4.317; P<0.04 for the interaction term). Age- and heart rate-adjusted E/A velocity ratio at transmitral Doppler examination was lower in women in the presence of the MS (P=0.064), whereas no difference was found among men. However, no significant interaction between sex and the MS was observed.

Discussion

Previous studies have shown that the MS is associated with elevated LV mass. This study confirms those findings in a large sample of subjects with essential hypertension. However, the main new finding of the present study is that a remarkable sex difference exists in the association between the MS and LV hypertrophy. Indeed, in the present study, Adult Treatment Panel III–defined MS was a strong determinant of LV mass in women beyond the influence of body size and hemodynamic variables, whereas the relation was weaker and fully explained by the effect of confounding factors in men.

We have observed previously that the association with LV mass of 2 of the components of the MS, that is, low high-density lipoprotein cholesterol and elevated triglycerides, was somewhat stronger in women than in men. In the Hoorn study, impaired glucose metabolism and type 2 diabetes mellitus have been associated with increased LV mass in women, but not in men, although in that work, LV mass was normalized for body surface area, a measure that includes body fat, and this might not be the most appropriate indexation, because it tends to exclude the effects of obesity on LV mass. Sex-specific relations between LV mass and insulin resistance, estimated by the homeostasis model assessment, have been examined in the Framingham Heart Study. In that article, a relation between insulin resistance and LV mass was found only among women, but the difference was no longer significant after adjustment for body mass index. In a large black cohort of the Atherosclerosis Risk in Communities Study, components of the MS were associated with increased LV mass. Of note, hypertension had the strongest influence on LV mass, and an additional contribution of dyslipidemia and glucose intolerance (including diabetes) was described only in women but not in men. This is generally in line with our results. In that study, however, as many as 23% of the population had frank diabetes, a well-known determinant of LV hypertrophy, and it cannot be excluded that diabetes played a leading role in the observed association between metabolic factors and LV mass. Moreover, black people have

TABLE 3. Independent Predictors of LV Mass Index (g m⁻²) in Hypertensive Women and Men in a Stepwise Linear Regression Model

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>β</th>
<th>Multiple R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women (n=253)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.85</td>
<td>0.35</td>
<td>0.44</td>
<td>&lt;0.001</td>
</tr>
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<td>Age, y</td>
<td>0.27</td>
<td>0.28</td>
<td>0.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24-h systolic BP, mm Hg</td>
<td>0.16</td>
<td>0.22</td>
<td>0.59</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MS, yes/no</td>
<td>4.80</td>
<td>0.19</td>
<td>0.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men (n=365)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.97</td>
<td>0.36</td>
<td>0.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24-h systolic BP, mm Hg</td>
<td>0.29</td>
<td>0.33</td>
<td>0.52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, y</td>
<td>0.20</td>
<td>0.20</td>
<td>0.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking, yes/no</td>
<td>2.12</td>
<td>0.09</td>
<td>0.61</td>
<td>0.048</td>
</tr>
<tr>
<td>MS, yes/no</td>
<td></td>
<td></td>
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<td>0.20</td>
</tr>
</tbody>
</table>

Diastolic BP, heart rate, serum cholesterol, serum creatinine, duration of hypertension, and alcohol intake were included in the model but failed to enter the final equations.

Discussion

Previous studies have shown that the MS is associated with elevated LV mass. This study confirms those findings in a large sample of subjects with essential hypertension. However, the main new finding of the present study is that a remarkable sex difference exists in the association between the MS and LV hypertrophy. Indeed, in the present study, Adult Treatment Panel III–defined MS was a strong determinant of LV mass in women beyond the influence of body size and hemodynamic variables, whereas the relation was weaker and fully explained by the effect of confounding factors in men.

We have observed previously that the association with LV mass of 2 of the components of the MS, that is, low high-density lipoprotein cholesterol and elevated triglycerides, was somewhat stronger in women than in men. In the Hoorn study, impaired glucose metabolism and type 2 diabetes mellitus have been associated with increased LV mass in women, but not in men, although in that work, LV mass was normalized for body surface area, a measure that includes body fat, and this might not be the most appropriate indexation, because it tends to exclude the effects of obesity on LV mass. Sex-specific relations between LV mass and insulin resistance, estimated by the homeostasis model assessment, have been examined in the Framingham Heart Study. In that article, a relation between insulin resistance and LV mass was found only among women, but the difference was no longer significant after adjustment for body mass index. In a large black cohort of the Atherosclerosis Risk in Communities Study, components of the MS were associated with increased LV mass. Of note, hypertension had the strongest influence on LV mass, and an additional contribution of dyslipidemia and glucose intolerance (including diabetes) was described only in women but not in men. This is generally in line with our results. In that study, however, as many as 23% of the population had frank diabetes, a well-known determinant of LV hypertrophy, and it cannot be excluded that diabetes played a leading role in the observed association between metabolic factors and LV mass. Moreover, black people have

TABLE 4. Multivariate-Adjusted Values of LV Mass Index (g m⁻²) in Hypertensive Men and Women Subdivided by Presence or Absence of the Single Components of the MS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Absent</th>
<th>Present</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low HDL cholesterol</td>
<td>41.7 (n=202)</td>
<td>46.0 (n=51)</td>
<td>0.004</td>
</tr>
<tr>
<td>High triglycerides</td>
<td>41.6 (n=188)</td>
<td>45.3 (n=65)</td>
<td>0.006</td>
</tr>
<tr>
<td>High waist circumference</td>
<td>41.2 (n=125)</td>
<td>43.7 (n=128)</td>
<td>0.07</td>
</tr>
<tr>
<td>High fasting glycemia</td>
<td>42.4 (n=241)</td>
<td>45.4 (n=12)</td>
<td>0.28</td>
</tr>
</tbody>
</table>

LV mass index values are adjusted for age, body mass index, average 24-h systolic blood pressure, smoking, and alcohol intake.
a greater prevalence of metabolic disorders36 and cardiac hypertrophy,37 and findings obtained in blacks may not be extended to a white population. To the best of our knowledge, the present study is the first to explore directly the influence of sex on the association between the MS and cardiac structure and function in white subjects.

The possible mechanisms underlying the interaction of sex on the association between the MS and LV mass remain hypothetical. Increased large-artery stiffness, a correlate of the MS in hypertension,38 might contribute to increase LV mass by elevating cardiac afterload. However, the increase in LV mass in women was found to be independent of increased arterial stiffness in the Hoorn Study.33 Moreover, insulin resistance might counterbalance the favorable cardiovascular effects of estrogen in women,39 thus canceling some of their effects on LV mass.40 Our finding of a strong effect of the MS on cardiac structure both before and after menopause seems to support this hypothesis. Further studies are needed to elucidate the potential explanations of the present findings.

In the present study, we have demonstrated a link between the MS and a cluster of LV geometric and functional abnormalities, which might provide prognostic information beyond the contribution of LV mass in subjects with essential hypertension.29,31,40,41 Indeed, in our study, women with the MS had a concentric LV geometric pattern,41 a prolonged LV relaxation,31 a reduced midwall systolic function,29 and a higher proportion of inappropriately high LV mass, that is, values of LV mass exceeding levels needed to compensate hemodynamic load.42

Study Strengths and Limitations

In this study, exclusion of subjects with overt cardiovascular disease, diabetes, and previous or current antihypertensive treatment allowed us to eliminate the influence of several major confounding factors. Moreover, the well-established influence of BP values on the association between MS and LV mass was excluded by adjustment for the effect of average 24-hour BP (Tables 3 and 4), a stronger predictor of cardiovascular risk than office BP in hypertension.43 Our cross-sectional investigation does not permit any causal inferences. This study was carried out in a population of white adult hypertensive patients, and results may not be directly applicable to the general population and to other ethnicities. However, high BP is by far the most frequent component of the MS and, in the general population, >90% of the subjects with MS have increased BP.44 Although prevalence of the MS was slightly underestimated by focusing on participants with valid echocardiograms in the present study, recent evidence suggests that cardiovascular risk does not differ for those with adequate and inadequate echocardiograms.45

Perspectives

Our findings that LV hypertrophy and several patterns of subclinical hypertensive heart disease are present in hypertensive women with the MS over and above the confounding effect of 24-hour BP, as well as several hemodynamic and nonhemodynamic factors, have important clinical and public-health implications. Indeed, echocardiographically determined LV hypertrophy has been implicated as a major contributor to cardiovascular disease outcomes in essential hypertension.12,13 These results are in line with several previous studies showing that women with diabetes lose their advantage over men in terms of cardiovascular disease46 and extend those findings to nondiabetic hypertensive subjects with the MS.

Acknowledgments

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Different Impact of the Metabolic Syndrome on Left Ventricular Structure and Function in Hypertensive Men and Women
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