Furthermore, in agreement with the other study quoted by Protogerou et al.,8 showing that arterial stiffening by MS is more pronounced in hypertensive women than men, we found, in our overall study population, a greater difference of age-adjusted clinic PP between subjects with and without MS in women (68 ± 16 mmHg; P = .004) than in men (61 ± 16 mmHg; P = .03).

### Table 1. Clinic heart rate and sex distribution of hypertensive patients with (+) and without (−) metabolic syndrome (MS) belonging to the second and third tertiles of the age distribution

<table>
<thead>
<tr>
<th>II tertile of age (41–51 years)</th>
<th>III tertile of age (&gt;51 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MS+ (n = 74)</strong></td>
<td><strong>MS+ (n = 89)</strong></td>
</tr>
<tr>
<td>Sex (male/female), %</td>
<td>Sex (male/female), %</td>
</tr>
<tr>
<td>Clinic heart rate (beats/min)</td>
<td>Clinic heart rate (beats/min)</td>
</tr>
<tr>
<td>74.4 ± 8.7^NS</td>
<td>74.3 ± 7.9^NS</td>
</tr>
<tr>
<td>48/52*</td>
<td>46/54*</td>
</tr>
<tr>
<td><strong>MS− (n = 102)</strong></td>
<td><strong>MS− (n = 86)</strong></td>
</tr>
<tr>
<td>74.3 ± 8.5</td>
<td>72.6 ± 8.9</td>
</tr>
<tr>
<td>66.6/33.3</td>
<td>64/36</td>
</tr>
</tbody>
</table>

NS = not significant v MS−; 
* P < .05 v MS−.


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**Endothelial Dysfunction and Preeclampsia**

*To the Editor:*

We read with great interest the recent article by Garcia et al in the *American Journal of Hypertension*.1 They studied and followed (by telephone) a large number of Colombian women <25 years of age (n = 440) and found a prevalence of pregnancy-induced hypertension (PIH) of 6.32%. However, the authors described (in Methods) that two control subjects for every case of PIH were randomly selected, basically to optimize resources, reducing immediately the studied population from 506 to 96 women. Garcia et al showed that women who later developed PIH had significantly higher concentrations of C-reactive protein (CRP) and leukocyte counts, while flow-mediated dilation (FMD) was lower than in controls. The authors concluded that an association existed between those values and the risk of preeclampsia (PE). It is also consistent with their hypothesis of endothelial dysfunction because of systemic inflammation during PE. In that sense, in a much larger prospective follow-up study of 207 Ecuadorian women (11.6% with PE; age, <25 years) that measured high-sensitivity latex CRP every 4 weeks starting at week 16 of pregnancy, we found that although CRP increased more during pregnancy in women who later developed PE than in normotensive women, it had no predictive value for PE.2 Moreover, in some of these women, plasma nitric oxide (NO) was also measured every 4 weeks, and we found that NO varied between those women with PE and their controls and, more interestingly, that lower levels of NO in early pregnancy were associated with a risk 13 times higher for the future development of PE.3 Therefore, we agree with Garcia et al1 that endothelial dysfunction during early pregnancy might be responsible for the future development of PE, but our results4,5 strongly suggest that early abnormal placentation, rather than inflammatory re-

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**References**

sponse, might be the most important alteration for the late development of PE.

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References

Reply to: Endothelial Dysfunction and Preeclampsia

To the Editor:
We thank Teran et al for their interest in our study. We agree with their assertion that an early abnormal placenta might be one of the main factors involved in the pathogenesis of preeclampsia. Placental ischemia and hypoxia, resulting from a defect in placental trophoblast invasion during implantation and an inadequate remodeling of the uterine spiral arteries, lead to the release of inflammatory stimuli into the maternal circulation, involving lipid peroxidation and the stimulation of proinflammatory cytokine production by the placenta. A recent report also showed that human placental tissue has the ability to synthesize and release acute-phase proteins such as C-reactive protein (CRP). In addition, some large studies suggested that elevated CRP levels could be an independent predictor of preeclampsia. This association was highly correlated with prepregnancy adiposity and body mass index. Qiu et al, in a prospective, nested, case-control study, reported that pregnant women with higher concentrations of CRP presented an increased risk of preeclampsia. This correlation reached statistical significance only in lean pregnant women, but no similar association was observed in overweight women. This close relationship between adiposity and CRP levels provides a possible explanation for the lack of a predictive value of CRP in studies that do not take into account these variables. In our study, pregnant women were matched by body mass index, guaranteeing that the observed differences were not related to adiposity levels.

In conclusion, the available data support the hypothesis that poor placentation might be the cause of a generalized intravascular inflammatory reaction and a state of increased oxidative stress that produce endothelial dysfunction early in pregnancy and predispose women to a higher risk of developing preeclampsia. However, we think that several other factors, such as nutritional deficiencies, subclinical infections, metabolic disorders, and ethnic differences, also need to be evaluated in the study of etiologic factors in the endothelial dysfunction characteristic of preeclampsia, especially in developing countries.

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