Metabolic Syndrome Is Associated With Silent Ischemic Brain Lesions

Hirokazu Bokura, MD; Shuhei Yamaguchi, MD; Kenichi Iijima, MD; Atsushi Nagai, MD; Hiroaki Oguro, MD

Background and Purpose—Metabolic syndrome (MetS) is a recognized risk factor for stroke, but it is unclear whether MetS is also related to subclinical ischemic lesions. We examined the association of MetS with the prevalence of silent brain infarction, periventricular hyperintensity, and subcortical white matter lesions in healthy adults.

Methods—We conducted a cross-sectional study in 1151 Japanese healthy subjects. Three types of silent lesions were assessed by MRI scans. MetS was diagnosed using the criteria by the National Cholesterol Education Adult Treatment Panel III.

Results—After adjusting for age and other factors, MetS was significantly associated with silent brain infarction, periventricular hyperintensity and subcortical white matter lesions. Among the MetS components, elevated blood pressure was commonly associated with all types of lesions. Dyslipidemia and elevated fasting glucose levels were associated with subcortical white matter lesions and periventricular hyperintensities, respectively. Positive trends were observed between the number of MetS components and prevalence of silent lesions.

Conclusions—MetS is associated with the prevalence of silent lesions independent of other risk factors. The clustering of MetS components tends to increase the prevalence of silent lesions. (Stroke. 2008;39:000-000.)

Key Words: metabolic syndrome ■ silent brain infarction ■ periventricular hyperintensity ■ subcortical white matter lesions

Prospective population-based cohort studies have demonstrated that metabolic syndrome (MetS) is a potent risk factor for stroke.1,2 Very few studies have investigated the influence of MetS on silent ischemic brain lesions,3,4 although they are regarded as warning signs for future stroke and cognitive deterioration.5 In this study we investigated the association of MetS and 3 types of subclinical ischemic lesions: silent brain infarction (SBI), periventricular hyperintensity (PVH), and subcortical white matter lesions (SWMLs).

Materials and Methods

Subjects
We studied 1151 healthy persons (44 to 87 years) selected from 1518 Japanese adults, who voluntarily visited the Shimane Institute of Health Science for health screening. The screening system included medical and neurological examination, head MRI scans, and blood tests. The selection criteria were as follows: informed consent to this study, no history of psychiatric or neurological diseases including transient ischemic attack, no neurological abnormalities, and no missing data for complete analysis. Demographic data are shown in Table 1. The study was approved by the institutional ethics committee.

Criteria of Metabolic Syndrome
MetS was diagnosed based on the criteria from the National Cholesterol Education Program Adult Treatment Panel III,6 modified for the Japanese people.7 Although waist circumference is the preferred measure of central obesity in MetS diagnosis, it was not measured at the time of data acquisition. For this reason, we used body mass index (BMI) as a substitute for waist circumference. The good correlation between them was obtained in a separate study.8 Central obesity was defined as BMI ≥25.

Magnetic Resonance Imaging
Head MRIs were obtained using conventional pulse sequences for T2-weighted image, T1-weighted image, and fluid-attenuated inversion recovery (FLAIR) image in the transverse plane with a slice thickness of 7 mm by a 1.5-Tesla MRI (Symphony, Siemens).

Silent Brain Lesions
Brain infarction was defined as a focal hyperintensity lesion 3 mm or large in diameter in the T2-weighted image corresponding to a hypointensity lesion in the T1-weighted image. PVH and SWMLs were evaluated separately based on their distinct subcortical distributions. PVH was graded on a scale of 0 to 4 as described elsewhere.9 SWMLs were graded on a scale of 0 to 3 according to the Fazekas’ grading scheme.10 We defined grades 0 to 2 PVH as PVH−, grades 3 to 4 PVH as PVH+, grades 0 to 1 SWML as SWML−, and grades 2 to 3 SWML as SWML+. 

Statistical Analysis
We used Student t test, the Mann–Whitney U test, or χ2 test in the group comparison. Logistic regression models were used to determine the association between silent lesions and risk factors or MetS
Components and Silent Brain Lesions

Table 1. Demographic Data and Prevalence of MetS Components and Silent Brain Lesions

<table>
<thead>
<tr>
<th></th>
<th>Non-MetS (n=1030)</th>
<th>MetS (n=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female</td>
<td>519/511</td>
<td>96/25*</td>
</tr>
<tr>
<td>Age, y</td>
<td>62.6±6.5</td>
<td>62.7±7.9</td>
</tr>
<tr>
<td>Education, y</td>
<td>12.3±2.6</td>
<td>12.5±2.7</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>33.4</td>
<td>54.5*</td>
</tr>
<tr>
<td>Alcohol habit, %</td>
<td>14.0</td>
<td>26.4†</td>
</tr>
<tr>
<td>Increased BMI, %</td>
<td>14.6</td>
<td>100*</td>
</tr>
<tr>
<td>Elevated blood pressure, %</td>
<td>40.2</td>
<td>91.0*</td>
</tr>
<tr>
<td>Dyslipidemia, %</td>
<td>21.7</td>
<td>62.3*</td>
</tr>
<tr>
<td>Only TG &gt;150 mg/dL, %</td>
<td>19.0</td>
<td>50.0*</td>
</tr>
<tr>
<td>Only HDL &lt;40 mg/dL, %</td>
<td>1.2</td>
<td>1.6</td>
</tr>
<tr>
<td>Both above, %</td>
<td>1.5</td>
<td>10.7*</td>
</tr>
<tr>
<td>Elevated fasting glucose, %</td>
<td>22.0</td>
<td>63.1*</td>
</tr>
<tr>
<td>SBI +, %</td>
<td>11.6</td>
<td>27.9*</td>
</tr>
<tr>
<td>PVH +, %</td>
<td>4.0</td>
<td>8.2*</td>
</tr>
<tr>
<td>SWMLs +, %</td>
<td>15.1</td>
<td>25.4*</td>
</tr>
</tbody>
</table>

TG indicates triglycerides; HDL, high-density lipoproteins. Definitions of smoker and alcohol habit were described elsewhere.6

*p<0.0001, †p=0.0003.

components. The trend analysis was performed for the association between the number of MetS components and silent lesions by assigning median values for the odds ratio for each category. P<0.05 was considered significant.

Results

MetS was more prevalent in men compared to women, and was associated with higher rates of smoking and alcohol consumption. Univariate logistic analyses revealed significant associations between MetS and SBI, PVH, or SWMLs (Table 2). Increased age, male sex, and smoking were significantly associated with SBI, whereas age was the only significant risk factor for PVH and SWMLs. Multivariate logistic analyses revealed that MetS was an independent risk factor for all 3 types of silent lesions.

Table 2 shows the effects of each MetS component on silent lesions. Multivariate logistic analyses revealed that increased BMIs, elevated blood pressure, and elevated fasting glucose were independent risk factors for SBI, elevated blood pressure and elevated fasting glucose for PVH, and elevated blood pressure and dyslipidemia for SWMLs.

The association between the number of MetS components and silent lesions are shown in Table 3. The prevalence of silent lesions was positively associated with the number of MetS components (P=0.008 for SBI and P<0.1 for PVH and SWMLs). These results did not change after adjusting for sex, age, or smoking habits. The inclusion of interactive variables across MetS components in the regression model showed no significant effects on the prevalence of silent lesions.

Discussion

We found that MetS was associated with 3 major silent ischemic brain lesions. Although age was most strongly associated with all silent lesions, MetS was still an independent risk factor after the adjustment of age. This finding is important because PVH and SWMLs are considered risk factors for future cognitive impairment.5 Our study basically confirmed recent studies1,4 but showed that only marked PVH and SWMLs were associated with MetS. Age and hypertension are well established risk factors for PVH and SWMLs, but the histological changes underlying mild PVH are not always caused by ischemia.11

It is unclear how MetS is related to the pathology of small-artery disease, which is a major underlying pathology in silent lesions. It was reported that MetS contributed to both atherothrombotic and lacunar infarctions.12 Various metabolic disturbances may promote pathological changes in the arteries, which usually begin in larger extracerebral arteries and then spread to smaller, distal, intracerebral arteries.1
The limitation of this study includes bias in subject selection due to nonrandomized design. Furthermore, longitudinal studies are obviously needed in the future for leading more general conclusions.

In conclusion, MetS was significantly associated with all 3 types of silent lesions after adjusting for age and other factors. The positive trend between MetS components and silent lesions could be used as a diagnostic tool to predict and prevent future stroke.

Sources of Funding
This study was supported by the Shimane Institute of Health Science.

Disclosures
None.

References

Table 3. Association of MetS Components With SBI, PVH, and SWMLs

<table>
<thead>
<tr>
<th>No. of MetS components</th>
<th>SBI</th>
<th>PVH</th>
<th>SWML</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1</td>
<td>1.49 (0.93–2.46)</td>
<td>1.75 (0.74–4.15)</td>
<td>1.04 (0.68–1.59)</td>
</tr>
<tr>
<td>2</td>
<td>2.00 (1.19–3.37)</td>
<td>2.14 (0.88–5.25)</td>
<td>1.45 (0.93–2.26)</td>
</tr>
<tr>
<td>3</td>
<td>4.03 (2.28–7.14)</td>
<td>2.66 (0.94–7.50)</td>
<td>1.62 (0.93–2.81)</td>
</tr>
<tr>
<td>4</td>
<td>4.71 (2.11–10.5)</td>
<td>7.76 (2.53–23.8)</td>
<td>3.40 (1.62–7.12)</td>
</tr>
</tbody>
</table>

OR indicates odds ratio.
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