Association Between the Number of Cardiovascular Risk Factors and Each Risk Factor Level in Elementary School Children

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Background  Little is known regarding the association between numbers of cardiovascular (CV) risk factors and the level of each risk factor in elementary school children based on a longitudinal study.

Methods and Results  A descriptive study of 319 obese children aged 6–11 years who participated in a screening program for comorbidity of obesity between 2003 and 2005, and who participated in consecutive years thereafter, was performed. Abdominal obesity, hypertension, dyslipidemia (low high-density lipoprotein-cholesterol levels and/or high triglyceride levels), and raised fasting glucose levels were used as the CV risk factors. Metabolic syndrome and each CV risk factor were defined using the criteria newly established by a Task Force financed by the Health and Labour Science Research in Japan. An increase in the total number of CV risk factors implied a worsening of each CV risk factor level over a 1-year interval, and vice versa. Abdominal obesity in males and insulin resistance in females were prevalent in children who were at elementary school level.

Conclusions  We should assess not only obesity but all CV risk factor levels, because a cluster of risk factors implies a worsening of the individual risk factor levels in children as young as those in elementary school. (Circ J 2008; 72: 1594–1597)

Key Words: Longitudinal studies; Metabolic syndrome; Risk factors

Obesity accompanies a clustering of cardiovascular (CV) risk factors including abdominal obesity, impaired glucose tolerance, hypertension and dyslipidemia, which has been termed metabolic syndrome. Clustering of CV risk factors is strongly associated with an increase in CV events in adults. It is well known that an improvement or worsening of obesity is strongly associated with an improvement or worsening of other CV risk factors, such as impaired glucose tolerance, hypertension, and dyslipidemia in children, adolescents, and adults by cross-sectional analyses. However, little is known regarding the association between clustering of CV risk factors and the level of each CV risk factor in children based on a longitudinal study.

The aim of the present study was to determine whether a change in the total number of CV risk factors was associated with a change in the individual risk factor levels over a 1-year period in elementary school children.
Table 1 Characteristics of the Subjects

<table>
<thead>
<tr>
<th></th>
<th>Boys (n=213)</th>
<th>Girls (n=106)</th>
<th>Gender difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First visit</td>
<td>Second visit</td>
<td>p value&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>9.0±1.3</td>
<td>10.0±1.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>134±8</td>
<td>140±9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>43.8±8.6</td>
<td>49.4±9.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Body mass index</strong></td>
<td>24.0±2.1</td>
<td>24.8±2.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>RBW (%)</strong></td>
<td>43±10</td>
<td>43±12</td>
<td>0.93</td>
</tr>
<tr>
<td><strong>Waist (cm)</strong></td>
<td>77±8</td>
<td>80±7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Waist/height ratio</strong></td>
<td>0.57±0.04</td>
<td>0.57±0.04</td>
<td>0.93</td>
</tr>
<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
<td>111±11</td>
<td>110±12</td>
<td>0.38</td>
</tr>
<tr>
<td><strong>Diastolic BP (mmHg)</strong></td>
<td>63±9</td>
<td>62±10</td>
<td>0.48</td>
</tr>
<tr>
<td><strong>HDL-C (mg/dl)</strong></td>
<td>57±11</td>
<td>57±12</td>
<td>0.43</td>
</tr>
<tr>
<td><strong>Triglycerides (mg/dl)</strong></td>
<td>97 (89–105)</td>
<td>107 (99–115)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>FBG (mg/dl)</strong></td>
<td>87±6</td>
<td>86±6</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Insulin (μU/ml)</strong></td>
<td>11.1 (10.3–11.9)</td>
<td>12.6 (11.7–13.5)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>HOMA-IR</strong></td>
<td>2.4 (2.2–2.6)</td>
<td>2.7 (2.5–2.9)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Number of CV risks</strong></td>
<td>1.5±0.7</td>
<td>1.6±0.7</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Metabolic syndrome</strong></td>
<td>14 (6%)</td>
<td>18 (8%)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

RBW, relative body weight; BP, blood pressure; HDL-C, high-density lipoprotein-cholesterol; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; CV, cardiovascular.
<sup>a</sup>Statistical significance levels between the first and second visits in boys.
<sup>b</sup>Statistical significance levels between the first and second visits in girls.

The data for triglycerides, insulin, and HOMA-IR levels are expressed as the mean and 95% confidence interval in parentheses because the data were skewed.

Personal data would be maintained.

**Physical and Blood Biochemical Parameters**

We measured height, weight, waist circumference, systolic and diastolic blood pressures (BPs), high-density lipoprotein (HDL)-cholesterol levels, triglyceride levels, fasting glucose levels, and fasting insulin levels. The height, weight, and waist circumference of the children were measured at each individual’s doctor’s clinic. Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg. Body mass index (BMI) was calculated as: (weight in kg)/(height in m)². BP was measured 3 times and the lowest value was used. Waist circumference was measured to the nearest 0.1 cm at the umbilical level.

Blood samples were collected in the morning after an overnight fast at each clinic and examined at the Laboratory Center of the Kagoshima City Medical Association. Serum cholesterol levels were determined by the cholesterol oxidase-peroxidase method. Triglycerides were determined by the glycerol kinase-glycerol-3-phosphate oxidase-peroxidase method. Insulin concentrations were measured by a chemiluminescence immunological assay. The homeostasis model assessment of insulin resistance (HOMA-IR)<sup>13</sup> was used as a surrogate marker of insulin resistance and was calculated as follows: [fasting insulin (μU/ml)] x [fasting glucose (mg/dl)]/405.

**Definition of Individual CV Risk Factors and Metabolic Syndrome**

Metabolic syndrome was defined using the newly established criteria created by a Task Force, which was financed by the Health and Labour Science Research Grants in Japan<sup>14</sup>. The criteria set out that a person should be diagnosed as having metabolic syndrome when there is abdominal obesity plus any 2 of the following 3 individual factors: dyslipidemia (raised triglyceride levels and/or reduced HDL-cholesterol levels), hypertension, and raised fasting blood glucose. Each CV risk factor was defined by the same criteria: abdominal obesity (waist circumference ≥75 cm and/or waist/height ratio ≥0.5 for elementary school children), elevated BPs (systolic BP ≥125 mmHg and/or diastolic BP ≥70 mmHg), low HDL-cholesterol levels (<40 mg/dl), high fasting serum triglyceride levels (≥120 mg/dl), and high fasting serum glucose levels (≥100 mg/dl). The total number of CV risk factors in a subject was evaluated at the first and second visits.

**Statistical Analysis**

Variables that were not normally distributed were log transformed. Statistical significance of the mean values between groups was based on the Mann–Whitney test or the Wilcoxon’s signed-rank test, and that for prevalence of metabolic syndrome was based on Fisher’s exact probability test. To determine whether clustering of CV risk factors was associated with a worsening of the individual risk factor levels, multivariate regression analysis was performed with adjustment for age and gender. Here, the changes in the levels of CV risk factors between the 2 visits were used as dependent variables, and the change in the total number of CV risk factors, age, and gender were used as independent variables. All statistical analyses were performed using SPSS 15.0J<sup>®</sup> software (Tokyo, Japan). A level of p<0.05 was considered statistically significant.

**Results**

The final number of subjects in the study was 319 obese children, consisting of 213 boys and 106 girls. Characteristics of the subjects are shown in Table 1. The mean values of waist circumference and fasting blood glucose in boys were higher than those in girls. The mean value of fasting insulin in girls was higher than that in boys. Over the 1-year interval, the mean values of waist circumference, and triglyceride, insulin, and HOMA-IR levels had significantly worsened; however, %RBW was not significantly increased. Gender difference was present in some CV risk factors. Boys showed a significantly higher waist circumference level than girls at both visits (Table 1). In contrast, girls had significantly higher fasting insulin and HOMA-IR levels than boys.
The numbers of subjects with a change in the total number of CV risk factors of ≤ –1, 0, 1, and 2 were 74, 162, 73, and 10 children, respectively. Change in the total number of CV risk factors was independently associated with changes in several risk factor levels between visits by multivariate regression analysis after adjusting for age and gender, in the following order; diastolic BP (t value and p value, 8.31, p<0.0001, respectively), triglycerides (6.48 and p<0.0001), systolic BP (5.95, p<0.0001), waist circumference (5.88, p<0.0001), fasting insulin (2.95, 0.003), HDL-cholesterol (–2.52, p=0.01), %RBW (2.31, p=0.02), and HOMA-IR levels (2.30, p=0.02). Fig 1 clearly shows that an increase in the total numbers of CV risk factors is associated with a worsening of each risk factor level, and vice versa.

**Discussion**

The present study showed that an increase in the total number of CV risk factors was independently associated with changes in several risk factor levels between visits by multivariate regression analysis after adjusting for age and gender, in the following order; diastolic BP (t value and p value, 8.31, p<0.0001, respectively), triglycerides (6.48 and p<0.0001), systolic BP (5.95, p<0.0001), waist circumference (5.88, p<0.0001), fasting insulin (2.95, 0.003), HDL-cholesterol (–2.52, p=0.01), %RBW (2.31, p=0.02), and HOMA-IR levels (2.30, p=0.02). Fig 1 clearly shows that an increase in the total numbers of CV risk factors is associated with a worsening of each risk factor level, and vice versa.

From a cross-sectional analysis, Retnakaran et al reported that the levels of CV risk factors (BMI, waist circumference, systolic BP, fasting insulin levels, and HOMA-IR levels) increased with an increasing number of total CV risk factors in 236 children aged 10–19 years. From a case-control study among 122,051 workers with a mean age of 50 years old, Nakamura et al reported that the odds ratio for the presence of ischemic heart disease significantly increased with an increasing number of total CV risk factors (obesity, hypertension, hyperglycemia, and hypercholesterolemia). However, little is known about the association between the total number of CV risk factors and the level of each CV risk factor in children based on a longitudinal study. The present study showed that an increase in the total number of CV risk factors implied a worsening of each CV risk factor level over a 1-year interval, and vice versa.

The present study showed gender differences in the presence of CV risk factors. A significantly higher waist circumference level in boys and significantly higher fasting insulin and HOMA-IR levels in girls indicated that abdominal obesity in males and insulin resistance in females were prevalent in children who were at elementary school level, which has also been shown in other studies.

The approach used in the present study had limitations. The present study included a larger percentage of boys than...
girls. Recent increases in the prevalence of obesity during elementary school years have been shown in boys but not in girls in Japan, indicating that a focus on boys is justified. The reason for this rapid increase in the prevalence of obesity in boys needs further investigation.

In conclusion, we should assess not only obesity, but all CV risk factor levels, because a cluster of risk factors implies a worsening of individual risk factor levels in children as young as those in elementary school.

References