Hypertension is the Most Important Component of Metabolic Syndrome in the Association With Ischemic Heart Disease in Taiwanese Type 2 Diabetic Patients

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**Background** To evaluate the association between components of metabolic syndrome (MS) and ischemic heart disease (IHD) in Taiwanese patients with type 2 diabetes mellitus (T2DM).

**Methods and Results** A total of 1,296 (604 men and 692 women) subjects with T2DM aged 62.5±11.7 (14–87) years were studied. MS was defined using the World Health Organization modified criteria and included more than 2 of hypertension, obesity, dyslipidemia, and microalbuminuria. IHD was diagnosed through history or ischemic electrocardiogram according to the Minnesota codes. Results showed that MS was present in 76.2% and IHD in 36.3% of the patients, respectively. MS increased with age for both sexes, but there was no difference between men and women in the age groups of <45, 45–54 and 55–64 years. However, the prevalence of MS was significantly higher in women (87.7% vs 78.0%) in the age group ≥65 years. IHD prevalence was significantly higher in patients with MS, hypertension, dyslipidemia and obesity (p<0.01), and was higher with borderline significance for microalbuminuria (0.05<p<0.1). The respective age-adjusted odds ratios were 3.61 (2.57–5.08), 7.10 (5.38–9.38), 1.70 (1.32–2.18), 1.75 (1.33–2.28), and 1.11 (0.88–1.41).

**Conclusions** The prevalence of MS in subjects with T2DM is high and increases with age. The impact of different risk factors on IHD is diverse, with hypertension being the most important. (Circ J 2008; 72: 1419–1424)

**Key Words:** Ischemic heart disease; Metabolic syndrome; Risk factors; Taiwan; Type 2 diabetes mellitus
deemed to be an issue. In addition, no significant differences in age or sex were noted among the main national sample, those who participated in the health examination or those selected patients with T2DM.

Risk Factors and Definition of MS

The WHO criteria for MS were used with modifications. Patients with ≥2 of the following risk factors: obesity, hypertension, dyslipidemia or microalbuminuria, were defined as having MS.

Measurement of anthropometric factors and blood pressure were described elsewhere. Obesity was defined as a BMI ≥25 kg/m² and/or a waist circumference (WC) ≥90 cm for men or ≥80 cm for women. These indicators are better predictors for MS, IHD and T2DM than the WHR indicator. Subjects were instructed to avoid any vigorous physical activities one day before the examination to prevent any undue influence on the excretion of urinary albumin. Urine and blood samples were collected in the early morning after subjects fasted for a minimum of 12h. First voided mid-stream urine was collected, then venous blood samples were collected. Urinary albumin concentrations were measured using a particle-enhanced turbidimetric immunoassay (Biolatex, Logroño, Spain). While, urinary creatinine concentrations were measured after dilution (×10) on an automated chemistry analyzer (Cobas Mira S, Roche Diagnostica, Basel, Switzerland) with reagents obtained from Randox Laboratories Ltd (Antrim, UK). ACRs ≥30 μg/mg were defined as microalbuminuria.

Diagnosis of IHD

Diagnosis of IHD was based on one of the following criteria: (1) definite history of acute myocardial infarction (self-reported with previous diagnosis made by a physician); (2) definite history of angina pectoris with documented electrocardiographic findings and under specific therapy (self-reported history of chest pain with confirmed diagnosis by an electrocardiogram done previously by a physician and being treated with medications including sublingual nitroglycerine, coronary vasodilators or antiplatelet agents (eg, aspirin, ticlopidine, dipyridamole or clopidogrel etc)]; (3) patients who had received a placement of coronary stents, percutaneous transluminal coronary angioplasty, coronary artery bypass graft or had tested positive after a coronary angiography examination, a treadmill exercise test or a radionuclide test; and (4) for those without any of the above medical history, a resting electrocardiogram was performed and coded according to the Minnesota codes. IHD was defined by the Minnesota codes of coronary probable (1.1, 1.2, 7.1) and coronary possible (1.3, 4.1–4.3, 5.1–5.3) as defined by the Whitehall criteria applied in the World Health Organization’s Multinational Study of Diabetes and Vascular Disease.

Statistical Analyses

Performing the Student’s t-test, the age between patients with and without IHD was compared and the chi-square test was used for the proportions of sex, smoking, hypertension, dyslipidemia and microalbuminuria. Because patients with IHD were significantly older than those without IHD, the differences of BMI, WC, SBP, DBP, FPG, HbA1c, TC, TG, HDL-C and LDL-C for those with and without IHD were compared by analysis of covariants (ANCOVA) adjusted for age.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>IHD No (n=826)</th>
<th>IHD Yes (n=470)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.4±12.5</td>
<td>66.0±9.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex (% men)</td>
<td>47.8</td>
<td>44.5</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>34.4</td>
<td>34.4</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>35.8</td>
<td>81.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>59.0</td>
<td>70.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity (%)</td>
<td>63.8</td>
<td>76.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Microalbuminuria (%)</td>
<td>50.3</td>
<td>55.2</td>
<td>0.09</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.6±3.4</td>
<td>25.2±3.8</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Waist circumference (cm) Men</td>
<td>88.5±8.6</td>
<td>91.5±8.9</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>131.7±16.4</td>
<td>135.3±14.8</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>79.5±23.5</td>
<td>80.4±9.8</td>
<td>NS*</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/L)</td>
<td>9.2±3.3</td>
<td>9.2±3.8</td>
<td>NS*</td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>8.1±3.0</td>
<td>8.0±1.9</td>
<td>NS*</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>5.5±4.0</td>
<td>5.6±3.7</td>
<td>NS*</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.9±1.8</td>
<td>2.2±2.1</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>High-density lipoprotein-cholesterol (mmol/L) Men</td>
<td>1.2±0.3</td>
<td>1.2±0.4</td>
<td>NS*</td>
</tr>
<tr>
<td>Low-density lipoprotein-cholesterol (mmol/L) Men</td>
<td>2.9±0.9</td>
<td>3.0±1.4</td>
<td>NS*</td>
</tr>
</tbody>
</table>

Data are means±standard deviation or %; NS (p>0.1); *age-adjusted p values by analysis of covariants. IHD, ischemic heart disease; NS, non-significant.
Prevalences of hypertension, dyslipidemia, obesity, microalbuminuria and MS in each age group and for both sexes were tested by linear test for trend and by chi-square test, respectively. Prevalences of IHD by the number of risk factors were tested by linear test for trend for the different age subgroups (<45, 45–54, 55–64 and ≥65 years) and for both sexes separately. Prevalences of IHD by age groups and by the different sexes were tested using a linear test for trend and chi-square test, respectively, in patients with a specific number of risk factors.

Prevalences of IHD with regards to the number of risk factors were tested by linear test for trend; and in those patients with and without MS, hypertension, dyslipidemia, obesity and microalbuminuria by chi-square test. Logistic regression models were created to estimate the unadjusted and the age-adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) for IHD for the presence vs the absence of MS, hypertension, dyslipidemia, obesity and microalbuminuria; and for the subgroups of patients having 1, 2, 3 and 4 risk factors vs those without any risk factors.

In order to evaluate the relative impact of each risk factor of the MS on IHD, a logistic regression model including all 4 risk components of the MS, ie, hypertension, dyslipidemia, obesity and microalbuminuria, and other potential confounders such as age, sex, smoking, FPG and HbA1c was created.

Data were expressed as a mean and standard deviation or percentage. P<0.05 was considered statistically significant, and 0.05≤p<0.1 borderline significant.

Results

Table 1 compares the baseline characteristics between patients with and without IHD. Since patients with IHD were older than those without, the p values comparing the other continuous variables were analyzed using ANCOVA adjusted for age. IHD patients showed no gender differences. Subjects with IHD were more obese in terms of BMI or WC. The percentage of patients with hypertension and dyslipidemia was higher in patients with IHD. SBP was higher in patients with IHD, but DBP was comparable. For lipid profile, only TG was significantly higher in patients with IHD, and the other lipid parameters did not differ significantly. The percentage of microalbuminuria was higher in patients with IHD with borderline significance. Smoking and glycemic control, as indicated by FPG or HbA1c, were not significantly different.

Prevalences of hypertension and MS on IHD
creased with that of increasing age in diabetic women. The prevalence of dyslipidemia showed no significant increasing trend with age in either sex. Differences in prevalences of MS and for the individual risk factors in each age stratum were not significantly different for both sexes, except for obesity in the age groups of 45–54, 55–64 and ≥65 years, and for microalbuminuria and MS in the age group ≥65 years.

Table 3 shows the age- and sex-specific prevalences of IHD by number of risk factors. Except for the age group <45 years, IHD increased significantly with increasing number of risk factors in all other age groups and in both sexes.

Table 4 shows the prevalences of IHD in different subgroups of patients with different risk classifications and the respective ORs for IHD before and after adjustment for age. As shown in the table, 987 patients (76.2%) had MS. Of the 4 risk factors, hypertension was the most significant, with a 7-fold higher risk of IHD than those not suffering from hypertension. Microalbuminuria was the least significant, with ORs of borderline significance. However, the risk of IHD increased in conjunction with increasing number of risk factors.

Table 5 shows the mutually adjusted ORs for IHD in a logistic regression model. Age, hypertension, dyslipidemia and obesity were significantly associated with IHD while the others were not.

**Discussion**

The high prevalence of MS (76.2%) is comparable to those reported in diabetic patients of other ethnicities. Patients with MS had a 3- to 4-fold higher risk of IHD (Table 4). However, hypertension seemed to be the most significant risk factor and microalbuminuria the least (Tables 4 and 5). This result of microalbuminuria being the least significant risk factor seems at odds with a study carried out in Finland and Sweden, where microalbuminuria conferred the strongest risk of cardiovascular death. The reason for this discrepancy is not known. However, different ethnicities might experience different risk factors.

In one Japanese study, hypertension was a significant risk factor for the recurrence of coronary heart disease independent of age, sex, HbA1c, TC, BMI, smoking, family history and stenosis score, especially in patients with abnormal glucose tolerance and/or diabetes. In order to see whether hypertension conferred a greater risk to IHD in patients with MS, we calculated the OR for patients with MS and hypertension vs those with MS but without hypertension after adjusting for age, sex, smoking, FPG and HbA1c in a second-
The prevalence of MS in Taiwanese T2DM patients is 76.2% and increases with increasing age but does not differ much between men and women. Patients with MS have 3- to 4-fold higher risk of IHD. Among the 4 risk factors, hypertension, dyslipidemia, obesity and microalbuminuria, hypertension is the most significant and microalbuminuria the least. The impact of different risk factors on IHD is diverse. Therefore, it is important to estimate the risk of IHD based on individual risk factors.

Acknowledgments

The present study was partly supported by grants from the New Century Health Care Promotion Foundation, the Department of Health (DOH95-101-2041-MY2), the National Taiwan University Hospital Yun-Lin Branch (NTUH95-1001-MY2), the National Science Council (NSC-86-2314-B-002-225, NSC-87-2314-B-002-226, NSC-88-2314-B-002-227, NSC-89-2314-B-002-228, NSC-90-2314-B-002-229, NSC-91-2314-B-002-230, NSC-92-2314-B-002-231, NSC-93-2314-B-002-232, NSC-94-2314-B-002-233, NSC-95-2314-B-002-234, NSC-96-2314-B-002-061-MY2), Taiwan.

References


13. Tseng CH. Lipoprotein(a) is an independent risk factor for peripheral arterial disease in Chinese type 2 diabetic patients in Taiwan. Diabetes Care 2004; 27: 517–521.

