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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

Metabolic syndrome (MS) is characterized by a cluster of risk factors that increase the chance of cardiovascular disease (CVD). They include: glucose intolerance; hypertension; abdominal obesity; and dyslipidemia.[1] The World Health Organization (WHO) and the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III have separately proposed criteria for the clinical diagnosis of MS.[1,2] The WHO defines MS as a condition of insulin resistance and diabetes mellitus (DM) or impaired glucose tolerance with the presence of 2 or more of these components: obesity (body mass index (BMI) ≥30 kg/m^2 and/or waist-to-hip ratio (WHR) >0.9 and >0.85 for men and women, respectively); hypertension (blood pressure ≥140/90 mmHg); dyslipidemia (triglycerides (TG) ≥1.7 mmol/L [150 mg/dl] and/or high-density lipoprotein-cholesterol (HDL-C) <0.9 mmol/L [35 mg/dl] and <1.0 mmol/L [39 mg/dl] for men and women, respectively); and microalbuminuria (urinary albumin-to-creatinine ratio (ACR) ≥30 μg/mg).[1] The NCEP-ATP III criteria differ slightly with those of the WHO.[2]

Subjects with type 2 DM (T2DM) show the highest risk of MS and CVD. Therefore understanding any correlation between CVD risk and the number of risk factors in a dose-responsive pattern, or the binary classification of MS or the components of MS, could well differentiate those patients at risk of ischemic heart disease (IHD) from those not at risk. As a result, the purpose of the present study examines the relation between IHD and (1) each component of MS, (2) the number of components of MS and (3) MS itself, in T2DM cases.

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Methods

Study Subjects

The present study was approved by an ethics committee with subjects participating voluntarily. Taiwan has an established cohort of 93,484 confirmed diabetic patients derived from a national sample of 256,036 patients under National Health Insurance cover, which covers over 96% of the total population.[3,4] A health examination was planned for recruiting 1,400 patients from the main cluster. At random, 4,164 patients were selected from the main cluster and invited to participate in the health examination. A total of 1,441 patients accepted the invitation to this health examination and 1,420 patients were discovered to have T2DM. Among these T2DM patients, 1,296 patients (604 men and 692 women) had complete medical data for analyses in this present study. The mean age was 62.5±11.7 (14–87) years. All subjects were selected at random, thus a selection bias was not

Table 1 Comparisons of Characteristics Between Patients With and Without IHD

Characteristics	IHD No (n=826)	IHD Yes (n=470)	p value
Age (years)	60.4±12.5	66.0±9.9	<0.001
Sex (% men)	47.8	44.5	NS
Smoking (%)	34.4	34.4	NS
Hypertension (%)	35.8	81.5	<0.001
Dyslipidemia (%)	59.0	70.9	<0.001
Obesity (%)	63.8	76.6	<0.001
Microalbuminuria (%)	50.3	55.2	0.09
Body mass index (kg/m^2)	24.6±3.4	25.2±3.8	<0.01*
Waist circumference (cm)			
Men	88.5±8.6	91.5±8.9	<0.001*
Women	85.9±9.9	89.0±11.2	<0.001*
Systolic blood pressure (mmHg)	131.7±16.4	135.3±14.8	<0.001*
Diastolic blood pressure (mmHg)	79.5±23.5	80.4±9.8	NS*
Fasting plasma glucose (mmol/L)	9.2±3.3	9.2±3.8	NS*
Hemoglobin A_{1c} (%)	8.1±3.0	8.0±1.9	NS*
Cholesterol (mmol/L)	5.5±4.0	5.6±3.7	NS*
Triglyceride (mmol/L)	1.9±1.8	2.2±2.1	<0.01*
High-density lipoprotein-cholesterol (mmol/L)			
Men	1.2±0.3	1.2±0.4	NS*
Women	1.4±0.4	1.3±0.4	NS*
Low-density lipoprotein-cholesterol (mmol/L)	2.9±0.9	3.0±1.4	NS*

*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.

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.[5,6] Obesity was defined as a BMI ≥25 kg/m^2 and/or a waist circumference (WC) ≥90 cm for men or ≥80 cm for women.[7–9] These indicators are better predictors for MS, IHD and T2DM than the WHR indicator for CVD in T2DM patients in Taiwan.[5,10] Patients were defined as having hypertension if undergoing antihypertensive treatments; having systolic blood pressure (SBP) ≥140 mmHg; or showing diastolic blood pressure (DBP) ≥90 mmHg. Patients who smoked one or more cigarettes per day were defined as smokers.

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 12 h. 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).[11,12] 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. Fasting plasma glucose (FPG), hemoglobin A_{1c} (HbA_{1c}), serum total cholesterol (TC), TG, HDL-C and low-density lipoprotein-cholesterol (LDL-C) were measured as described.[11–13] Dyslipidemia was defined as a TG level ≥1.7 mmol/L and/or HDL-C <0.9 mmol/L for men or <1.0 mmol/L for women, or those undergoing treatment for lipid disorder.

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.[14] 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.[15]

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, HbA_{1c}, TC, TG, HDL-C and LDL-C for those with and without IHD were compared by analysis of covariants (ANCOVA) adjusted for age.

Table 2 Age- and Sex-Specific Prevalence of MS and Each Component of the Risk Factors

Sex/risk factors	*Age group (years)*					
	<45	*45–54*	*55–64*	*≥65*	*All*	*p value**
Men (n)	*49*	*110*	*185*	*261*	*605*	
Hypertension (%)	*19.1*	*38.0*	*50.3*	*57.1*	*48.6*	*<0.001*
Dyslipidemia, (%)	*57.4*	*63.0*	*59.6*	*62.2*	*61.1*	*>0.1*
Obesity (%)	*54.3*	*60.0*	*55.9*	*58.2*	*57.5*	*>0.1*
Microalbuminuria (%)	*48.9*	*46.2*	*49.2*	*53.2*	*50.3*	*>0.1*
MS (%)	*57.4*	*65.7*	*69.9*	*78.0*	*71.7*	*<0.01*
Women (n)	*56*	*93*	*198*	*344*	*691*	
Hypertension (%)	*14.8*	*48.4*	*54.1*	*64.9*	*55.6*	*<0.001*
Dyslipidemia (%)	*53.7*	*68.1*	*62.8*	*68.4*	*65.6*	*>0.1*
Obesity (%)	*61.5*	*73.9*	*79.3*	*82.0*	*78.5*	*<0.01*
Microalbuminuria (%)	*42.6*	*43.3*	*48.2*	*61.5*	*53.7*	*<0.01*
MS (%)	*57.4*	*74.7*	*75.5*	*87.7*	*80.1*	*<0.001*

**p values by trend test comparing the prevalence of MS and each component of the risk factors by increasing age.*
The p values by chi-square test comparing the differences in prevalences of MS and each component of the risk factors between men and women in each stratum of age are not significant (p>0.05), except for obesity in the age groups of 45–54, 55–64 and ≥65 years, and for microalbuminuria and MS in the age group of ≥65 years.
MS, metabolic syndrome.

Table 3 Age- and Sex-Specific Prevalence of IHD by Number of Risk Factors

Subgroups	*Number of risk factors*					*p value**
	0	*1*	*2*	*3*	*4*	
n	*68*	*241*	*393*	*387*	*207*	
Age, years						
<45	*14.3*	*10.3*	*8.8*	*16.7*	*33.3*	*>0.1*
45–54	*7.7*	*14.9*	*14.1*	*31.8*	*54.8*	*<0.0001*
55–64	*0*	*14.6*	*33.3*	*39.6*	*61.4*	*<0.0001*
≥65	*16.7*	*23.5*	*37.6*	*53.6*	*68.2*	*<0.0001*
*p values**	*>0.1*	*0.085*	*<0.0001*	*<0.0001*	*<0.05*	
Sex						
Men	*6.1*	*16.1*	*31.0*	*47.2*	*67.1*	*<0.0001*
Women	*15.8*	*17.9*	*29.1*	*44.2*	*59.7*	*<0.0001*
*p values***	*>0.1*	*>0.1*	*>0.1*	*>0.1*	*>0.1*	

**p values by trend test; **p values by chi-square test.*
Abbreviation see in Table 1.

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 HbA_{1c} 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 HbA_{1c}, were not significantly different.

Age- and sex-specific prevalences of MS and each component of the risk factors are shown in Table 2. Increasing prevalences of hypertension and MS with that of increasing age were observed in both sexes, respectively. In addition, the prevalences of obesity and microalbuminuria also in-

Table 4 Prevalences and ORs for IHD Among Subgroups of Patients With Different Risk Classifications

Risk classification	*n*	*IHD (%)*	*OR (95%CI)*	
			Unadjusted	*Age-adjusted*
Number of risk factors				
0	*68*	*8.8**	*1.00*	*1.00*
1	*241*	*17.0*	*2.12 (0.86–5.24)*	*1.96 (0.79–4.89)*
2	*393*	*30.0*	*4.43 (1.87–10.53)*	*3.70 (1.54–8.89)*
3	*387*	*45.5*	*8.62 (3.64–20.40)*	*6.80 (2.84–16.29)*
4	*207*	*62.3*	*17.09 (7.06–41.36)*	*14.26 (5.82–34.93)*
MS				
No	*309*	*15.2**	*1.00*	*1.00*
Yes	*987*	*42.9*	*4.18 (2.99–5.84)*	*3.61 (2.57–5.08)*
Hypertension				
No	*617*	*14.1**	*1.00*	*1.00*
Yes	*679*	*56.4*	*7.88 (6.00–10.35)*	*7.10 (5.38–9.38)*
Dyslipidemia				
No	*475*	*28.6**	*1.00*	*1.00*
Yes	*821*	*40.7*	*1.71 (1.34–2.18)*	*1.70 (1.32–2.18)*
Obesity				
No	*418*	*27.3**	*1.00*	*1.00*
Yes	*878*	*41.0*	*1.85 (1.42–2.40)*	*1.75 (1.33–2.28)*
Microalbuminuria				
No	*621*	*33.8+*	*1.00*	*1.00*
Yes	*675*	*38.4*	*1.22 (0.97–1.54)+*	*1.11 (0.88–1.41)+*

*+0.05<p<0.1; *p<0.01 (by linear test for trend or by chi-square test).*
OR, odds ratio; CI, confidence interval. Other abbreviations see in Tables 1,2.

Table 5 Mutually Adjusted ORs for IHD in a Logistic Regression Model

Risk factors	*Interpretation*	*Adjusted OR (95%CI)*	*p value*
Age	*Every 1-year increment*	*1.03 (1.02–1.05)*	*<0.001*
Sex	*Men vs women*	*0.96 (0.67–1.38)*	*>0.1*
Smoking	*Yes vs no*	*1.23 (0.84–1.78)*	*>0.1*
Fasting plasma glucose	*Every 1-mmol/L increment*	*1.02 (0.98–1.06)*	*>0.1*
Hemoglobin A1c	*Every 1% increment*	*0.99 (0.94–1.01)*	*>0.1*
Hypertension	*Yes vs no*	*7.26 (5.43–9.71)*	*<0.001*
Dyslipidemia	*Yes vs no*	*1.43 (1.08–1.91)*	*<0.05*
Obesity	*Yes vs no*	*1.61 (1.19–2.20)*	*<0.05*
Microalbuminuria	*Yes vs no*	*0.86 (0.66–1.14)*	*>0.1*

Abbreviations see in Tables 1,4.

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 risk classification 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 for all of the potential risk factors. 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.[16] 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.[16] 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, HbA_{1c}, TC, BMI, smoking, family history and stenosis score, especially in patients with abnormal glucose tolerance and/or diabetes.[17] 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 HbA_{1c} in a secondary analysis. The adjusted OR (95% CI) was 5.98 (4.30–8.32) with a p<0.001. In patients with only one risk factor of hypertension, dyslipidemia, obesity or microalbuminuria, respectively, only hypertension conferred significant risk for IHD while compared to those without any of the risk factors (data not shown). The different impact of risk factors on IHD (Tables 4 and 5) was very important in clinical practice because the risk of IHD could vary with different combinations of risk factors, and in patients with MS containing different components of risk factors.

Because microalbuminuria was not significantly associated with IHD after adjustment for confounders (Table 5), we reclassified the number of risk factors varying from 0 to 3 with regards to hypertension, dyslipidemia and obesity; and recalculated the age-adjusted ORs for IHD for the number of risk factors of 0, 1, 2 and 3. The respective adjusted ORs (95% CI) were 1.00, 1.48 (0.75–2.90), 3.67 (1.94–6.96) and 11.21 (5.85–21.48). However, in multivariate logistic regression models including both the number of risk factors and the various risk factors along with the adjustment for age, sex, smoking, FPG and HbA_{1c}, it was found that the number of risk factors and microalbuminuria were not associated with IHD with statistical significance and the respective adjusted ORs (95% CI) for hypertension, dyslipidemia and obesity were 7.23 (5.15–10.16), 1.43 (1.01–2.00) and 1.61 (1.14–2.29). A similar finding of a lack of association with the number of risk factors was noted when microalbuminuria was not considered as a risk factor in the calculation of the number of risk factors (data not shown). Therefore it was the sort of risk factor but not the number of risk factors that was important.

TG is the only significant lipid parameter associated with IHD (Table 1). This is compatible with most studies in Taiwan, showing TG as an independent and strong risk factor for atherosclerotic diseases.[18] However, it seems inappropriate to conclude that cholesterol is not important because in secondary analysis the prevalence of the use of statin in patients with IHD was significantly higher than in those without IHD (8.7% vs 3.8%, p<0.001).

Glycemic control seemed unimportant (Tables 1 and 5). This was further confirmed in secondary analyses estimating the ORs for FPG and HbA_{1c} in separate models, without adjustment for confounders and after adjustment for age, sex, smoking, hypertension, dyslipidemia, obesity and microalbuminuria. None of these ORs was statistically significant (data not shown).

Smoking is a risk factor for IHD in the diabetic patients in some studies.[19,20] The lack of an association in the present study (Tables 1 and 5) was consistent with our previous follow-up study for IHD incidence in patients with T2DM.[14] The effect of smoking might be more important in younger individuals than in the elderly.[21–23] Therefore the role of smoking on IHD in the diabetic patients with an average age of approximately 60 years in Taiwan requires further confirmation.[3]

There are some limitations. First, the participants all had T2DM, therefore the results might not be applicable to those without diabetes or to patients with type 1 DM. Second, selection bias could not be completely excluded because we did not have any evidence of a similar distribution of IHD between the participants of the present study and the main national cohort. Third, the temporal correctness of cause and effect could not be evaluated in this cross-sectional study.

Conclusions

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.

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References

1. WHO Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. World Health Organization: Geneva, 1999.
2. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; **285:** 2486–2497.
3. Tseng CH. Mortality and causes of death in a national sample of diabetic patients in Taiwan. *Diabetes Care* 2004; **27:** 1605–1609.
4. Tseng CH. Body mass index and blood pressure in adult type 2 diabetic patients in Taiwan. *Circ J* 2007; **71:** 1749–1754.
5. Tseng CH. Body composition as a risk factor for coronary artery disease in Chinese type 2 diabetic patients in Taiwan. *Circ J* 2003; **67:** 479–484.
6. Tseng CH. Sexual difference in the distribution of atherosclerotic risk factors and their association with peripheral arterial disease in Taiwanese type 2 diabetic patients. *Circ J* 2007; **71:** 1131–1136.
7. World Health Organization. International Obesity Taskforce and International Association for the Study of Obesity. The Asia–Pacific perspective: Redefining obesity and its treatment. Hong Kong: WHO, IOTF and IASO, 2000.
8. Tanchoco CC, Cruz AJ, Duante CA, Litonjua AD. Prevalence of metabolic syndrome among Filipino adults aged 20 years and over. *Asia Pac J Clin Nutr* 2003; **12:** 271–276.
9. Fujimoto WY, Newell-Morris LL, Grote M, Bergstrom RW, Shuman WP. Visceral fat obesity and morbidity: NIDDM and atherogenic risk in Japanese American men and women. *Int J Obes* 1991; **15**(Suppl 2)**:** 41–44.
10. Tseng CH, Chong CK, Lin BJ, Chen CJ, Tai TY. Atherosclerotic risk factors for peripheral vascular disease in non-insulin-dependent diabetic patients. *J Formosan Med Assoc* 1994; **93:** 663–667.
11. Tseng CH. Lipid abnormalities associated with urinary albumin excretion rate in Taiwanese type 2 diabetic patients. *Kidney Int* 2005; **67:** 1547–1553.
12. Tseng CH. Correlation of uric acid and urinary albumin excretion rate in patients with type 2 diabetes mellitus in Taiwan. *Kidney Int* 2005; **68:** 796–801.
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.
14. Fu CC, Chang CJ, Tseng CH, Chen MS, Kao CS, Wu TJ, et al. Development of macrovascular diseases in non-insulin-dependent-diabetics in northern Taiwan: A four-year follow-up study. *Diabetes Care* 1993; **16:** 137–143.
15. Diabetes Drafting Group. Prevalence of small vessel and large vessel disease in diabetic patients from 14 centres: The World Health Organization Multinational Study of Vascular Disease in Diabetics. *Diabetologia* 1985; **28**(Suppl)**:** 615–640.
16. Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001; **24:** 683–689.

17. Nakamura Y, Saitoh S, Takagi S, Ohnishi H, Chiba Y, Kato N, et al. Impact of abnormal glucose tolerance, hypertension and other risk factors on coronary artery disease. *Circ J* 2007; **71:** 20–25.
18. Pan WH, Chiang BN. Plasma lipid profiles and epidemiology of atherosclerotic diseases in Taiwan: A unique experience. *Atherosclerosis* 1995; **118:** 285–295.
19. Turner RC, Millns H, Neil HA, Stratton IM, Manley SE, Matthews DR, et al. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). *BMJ* 1998; **316:** 823–828.
20. Al-Delaimy WK, Manson JE, Solomon CG, Kawachi I, Stampfer MJ, Willett WC, et al. Smoking and risk of coronary heart disease among women with type 2 diabetes mellitus. *Arch Intern Med* 2002; **162:** 273–279.
21. Sakurai A, Oka S, Sekine J, Tanaka H, Nagasawa Y, Numao Y, et al. Changes of ischemic heart disease in Utsunomiya, Japan, over 10 years: A survey of primary care physicians. *Jpn Circ J* 1998; **62:** 675–679.
22. Ogawa K, Numao T, Iizuka M, Yanagisawa A, Yoshino H, Ishikawa K, et al. Angiographic and coronary risk factor analyses of Japanese patients with ischemic heart disease before age 40: A multicenter cooperative study. *Jpn Circ J* 1996; **60:** 822–830.
23. Horenstein RB, Smith DE, Mosca L. Cholesterol predicts stroke mortality in the Women's Pooling Project. *Stroke* 2002; **33:** 1863–1868.