Epidemiology

Clinical Identification of the Metabolic Syndrome in Kinmen

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Background: Metabolic syndrome is important to the global burden of cardiovascular disease. This study estimated the prevalence of metabolic syndrome in Kinmen, according to the clinical criteria from the Third Report of the National Cholesterol Education Program (ATP III).

Methods: A database of 8,320 men and women aged 30–92 years who participated in a community-based, cross-sectional survey was analyzed. According to ATP III, the diagnosis of the metabolic syndrome was made when Three or more of the following risk determinants were present: abdominal obesity (waist circumference: men 102; women > 88 cm), high triglycerides (150 mg/dL), low high-density lipoprotein cholesterol (men, < 40 mg/dL; women < 50 mg/dL), high blood pressure (130/ 85 mm Hg), and high fasting glucose (110 mg/dL).

Results: The prevalence of metabolic syndrome was significantly higher in women (878/4,716, 18.62%) than in men (405/3,604, 11.24%, $p = 0.001$). The prevalence of the components of metabolic syndrome for men and women were: abdominal obesity, 3.72% and 28.52%, respectively ($p = 0.001$); high triglycerides, 13.37% and 10.45% ($p = 0.001$); low high-density lipoprotein cholesterol, 20.98% and 37.66% ($p = 0.001$); high blood pressure, 61.07% and 43.74% ($p = 0.001$); and high fasting glucose, 23.25% and 19.64%, ($p = 0.001$). When abdominal obesity was redefined according to the cut-offs of waist circumferences > 90 cm for men or > 80 cm for women, the prevalence of metabolic syndrome remained significantly higher in women than in men (23.77% vs 17.73%; $p < 0.0001$).

Conclusion: The significant gender difference in the prevalence of metabolic syndrome in Kinmen is related to the higher prevalence of abdominal obesity and low high-density lipoprotein cholesterol in women than in men.

Key Words: Insulin resistance • Metabolic syndrome • Population-based study

INTRODUCTION

The clustering of cardiovascular risk factors, such as hypertension, glucose intolerance, high triglycerides and low high-density lipoprotein cholesterol concentrations, greatly enhances the future cardiovascular risk.[1, 2] Reaven et al[3] and others[4, 5] proposed that insulin resistance and the compensatory hyperinsulinemia may be the common underlying pathophysiology for the syndrome of a constellation of metabolic lipid and nonlipid risk factors. The various names (such as syndrome X,[3] insulin resistance syndrome,[5] metabolic syndrome X,[6] insulin resistance metabolic syndrome,[7] the deadly quartet,[8] and the metabolic syndrome[9]), and the constant addition of new components[10–13] to the syndrome imply the complexity of the syndrome as well as the difficulty for the definition. Since the increasing importance of the syndrome to the global burden of cardiovascular disease has been recognized,[14–16] a World Health Organization expert committee has recently proposed that the syndrome be referred to as 'The Metabolic Syndrome' and the metabolic syndrome should be diagnosed in patients who have glucose intolerance and/or insulin resistance together with two other components of the syndrome.[17] An operative definition of the metabolic syndrome should facilitate the investigation of its role in the development of cardiovascular disease and the relationship between insulin resistance and the other components of the syndrome.

More recently, the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in

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Adults (ATP III) has recognized the metabolic syndrome for targeting low-density lipoprotein cholesterol reduction, and secondarily, risk-reduction therapy for other risk factors.[18] A simplified approach to the clinical identification of the metabolic syndrome has been proposed, without the need for tests of insulin sensitivity or glucose tolerance.[18] Therefore, the aim of the present study was to estimate the prevalence of metabolic syndrome in Kinmen, based on the ATP III definition.

MATERIALS AND METHODS

Study population

Kinmen County of Taiwan has a population of around 45,000 residing on one principal island (Quemoy) and several nearby islets, all very close to the southern mainland of China.[19] During the period 1991–1995, all residents over 30 years of age in five major townships (Kin-Hu,[19] Kin-Chen,[20] Kin-Sa, Kin-Nin, and Lieh-Yu) in Kinmen were surveyed during summer and winter vacations by the Yang-Ming Crusade, a volunteer organization of the medical students from the National Yang-Ming University.[20] The overall response rate was 62.5%, in a target population of 20,185 based on household registrations. Because fasting serum insulin levels were not available during the pilot survey for Kin-Hu,[19] the data from the remaining four townships were used for the current investigation.

Demographic and clinical parameters including body height, body weight, body mass index (weight/height^2), waist-to-hip ratio,[21] systolic and diastolic blood pressures (average of three seated readings, separated by at least 5 minutes, after at least 10 minutes' rest) were documented via door-to-door interviews with a structured questionnaire.

Overnight fasting serum and plasma samples were drawn for glucose, insulin, lipid and other biochemical measurements. Fasting plasma glucose was determined by the hexokinase-glucose-6-phosphate dehydrogenase method with glucose (HK) reagent kit (Gilford, Oberlin, OH). Fasting serum insulin was measured by radioimmunoassay (Incstar Co., Stillwater, OK, USA). The detection limit was 2.05 U/mL. The intra- and inter-assay coefficients of variation were 7.4% and 9.1%, respectively.

Subjects with incomplete data were excluded from the current investigation. The final sample for this analysis consisted of 3,604 men and 4,716 women, with a mean age of 49.77 years (range: 30 to 92 years). This represented 52.72% (8,320/15,782) of all the respondents of the surveys.

The definition of metabolic syndrome was according to the ATP III recommendations[18] with some modification. The clinical components of the metabolic syndrome included abdominal obesity, triglycerides, high-density lipoprotein cholesterol, blood pressure, and fasting glucose.[18] According to ATP III criteria, the diagnosis of the metabolic syndrome was made when three or more of the following risk determinants were present: abdominal obesity (waist circumference: men, 102 cm; women, > 88 cm), high triglycerides (150 mg/dL), low high-density lipoprotein cholesterol (men, < 40 mg/dL; women < 50 mg/dL), high blood pressure (130/ 85 mmHg), and high fasting glucose (110 mg/dL). In this study, subjects who were regularly taking antihypertensive medications were counted as having high blood pressure, even if their blood pressure levels were < 130/85 mmHg (14 men and 24 women fulfilled this criteria). Similarly, subjects who were under regular treatment for diabetes mellitus were counted as having high fasting glucose, even if their fasting glucose levels were < 110 mg/dL (11 men and 15 women fulfilled this criterion). Because the ATP III criteria for abdominal obesity may not be appropriate for Chinese, we recalculated the prevalence of abdominal obesity and metabolic syndrome according to the cut-offs of waist circumferences > 90 cm for men and > 80 cm for women.[22]

Statistics

Data were analyzed with the Statistical Analysis System. The comparison of prevalence between men and women was done using the chi-square test. The association between age levels and the prevalence of metabolic syndrome was analyzed using the Cochran-Armitage test. Statistical significance was set at $p < 0.05$.

RESULTS

Prevalence of metabolic syndrome risk factors

The overall prevalence of the 5 risk factors defined by the ATP III in decreasing order were high blood pressure (51.26%), low high-density lipoprotein cholesterol (30.43%), high fasting glucose (21.21%), abdominal obesity (17.78%), and high triglycerides (11.88%), respectively. The prevalence of abdominal obesity defined

Table 1. Prevalence of the risk factors for the metabolic syndrome in Kinmen

Risk factors	Men		Women	
	n	%	*n*	%
Abdominal obesity	134	3.72	1,345	28.52**
Abdominal obesity†	928	25.75	2,417	51.25**
High triglycerides	495	13.73	493	10.45**
Low high-density lipoprotein cholesterol	756	20.98	1,776	37.66**
High blood pressure	2,201	61.07	2,063	43.74**
High fasting glucose	838	23.25	926	19.64**

*$p < 0.05$; **$p < 0.01$; †Abdominal obesity defined by Asian criteria: waist circumference > 90 cm in men and > 80 cm in women.

by Asian criteria was 40.21%. The prevalences of the individual risk factors in men and women are shown in Table 1. There was a significant gender difference in the distribution of the clinical risk components of the metabolic syndrome. Men had higher prevalences of high blood pressure and high fasting glucose than women did. In contrast, women had much higher prevalence of abdominal obesity (defined by either ATP III or Asian criteria), high triglycerides, and low high-density lipoprotein cholesterol than men did (Table 1).

Risk factor clustering and metabolic syndrome prevalence

Table 2 shows the cumulative prevalence of the five components for metabolic syndrome in men and women. Of men, 25.03% of the population had no risk factors and only 0.14% had all five risk factors. Similarly in women, 28.05% of the population had no risk factors and 1.82% had all five risk factors. The prevalence of metabolic syndrome, defined as the presence of three of the risk factors, were 11.24% in men, and 18.62% in women. The prevalence of the metabolic syndrome among women was significantly higher than that among men ($p < 0.001$). The prevalence of metabolic syndrome for the whole population was 15.42%.

Table 2. Clustering of the risk factors (defined by ATP III criteria) of metabolic syndrome in Kinmen

Number of risk factors	Men		Women	
	n	%	*n*	%
Zero	902	25.03	1,323	28.05
One	1,477	40.98	1,472	31.21
Two	820	22.75	1,043	22.12
Three	318	8.82	553	11.73
Four	82	2.28	239	5.07
Five	5	0.14	86	1.82**
< Three	3,199	88.76	3,838	81.38
≥ Three	405	11.24	878	18.62**
Total	3,604	100	4,716	100

*$p < 0.05$; **$p < 0.01$.

When the Asian criteria for the abdominal obesity were adopted, the prevalence of the metabolic syndrome was 21.16% (Table 3) and remained significantly higher in women than in men (23.77% vs 17.73%; $p < 0.0001$).

Age effect on prevalence of risk factors and metabolic syndrome

The prevalence of the risk factors and metabolic syndrome in each age group are summarized in Table 3. For the whole sample, the prevalence of each risk factor increased with age (all $p < 0.001$ for a linear trend). Nonetheless, there was a significant gender difference in the age effect on the prevalence of risk factors (Figure 1). The prevalence of abdominal obesity increased sharply with age in women ($p < 0.001$ for a linear trend) but only modestly in men ($p < 0.001$ for a linear trend, and $p < 0.0001$ for interaction) (Figure 1A). The prevalence of high triglycerides did not change significantly with age in men ($p = 0.067$ for a linear trend) but increased significantly with age in women ($p < 0.001$ for linear trend and $p < 0.0001$ for interaction) (Figure 1B). Similarly, the prevalence of low high-density lipoprotein cholesterol did not change significantly with age in men ($p = 0.382$ for a linear trend) but increased significantly with age in women ($p < 0.001$ for a linear trend and $p < 0.0001$ for interaction) (Figure 1C). The prevalence of high blood pressure increased significantly with age in men and women (both $p < 0.001$ for a linear trend) but the slope was steeper in women ($p < 0.0001$ for interaction) (Figure 1D). Similarly, the prevalence of high fasting glucose increased significantly with age in men and women (both $p < 0.001$ for linear trend) but the slope was steeper in women ($p < 0.0003$ for interaction) (Figure 1E). In addition, the two slopes crossed over around the age of 60 years.

Although the prevalence of metabolic syndrome increased with age in men and women, the prevalence in women was much higher than that in men, after the age of 50 years ($p < 0.0001$ for interaction) (Figure 1F).

When abdominal obesity was redefined according to the cut-offs of waist circumference > 90 cm in men or > 80 cm in women, the changes of the prevalence of abdominal

Table 3. Prevalence of metabolic syndrome and its components stratified by age groups

Variable	30–40 N (%)	40–50 N (%)	50–60 N (%)	60–70 N (%)	70+ N (%)	Total
Abdominal obesity	180 (07.58)	285 (14.28)	370 (19.25)	391 (29.73)	253 (35.63)	1479 (17.78)**
Abdominal obesity†	588 (24.76)	779 (39.03)	855 (44.48)	695 (52.85)	428 (60.28)	3345 (40.21)**
High triglycerides	187 (07.87)	225 (11.27)	222 (11.55)	225 (17.11)	129 (18.17)	988 (11.88)**
Low high-density lipoprotein cholesterol	670 (28.21)	580 (29.06)	544 (28.30)	473 (35.97)	265 (37.32)	2532 (30.44)**
High blood pressure	749 (31.54)	938 (46.99)	1146 (59.63)	890 (67.68)	541 (76.20)	4264 (51.26)**
High fasting glucose	247 (10.40)	351 (17.59)	493 (25.65)	428 (32.55)	245 (34.51)	1764 (21.21)**
Metabolic syndrome	134 (5.64)	234 (11.72)	333 (17.33)	366 (27.83)	216 (30.42)	1283 (15.42)**
Metabolic syndrome†	218 (9.18)	350 (17.54)	459 (23.08)	454 (34.52)	279 (39.30)	1760 (21.16)**

†Abdominal obesity defined by Asian criteria: waist circumference > 90 cm in men and > 80 cm in women.

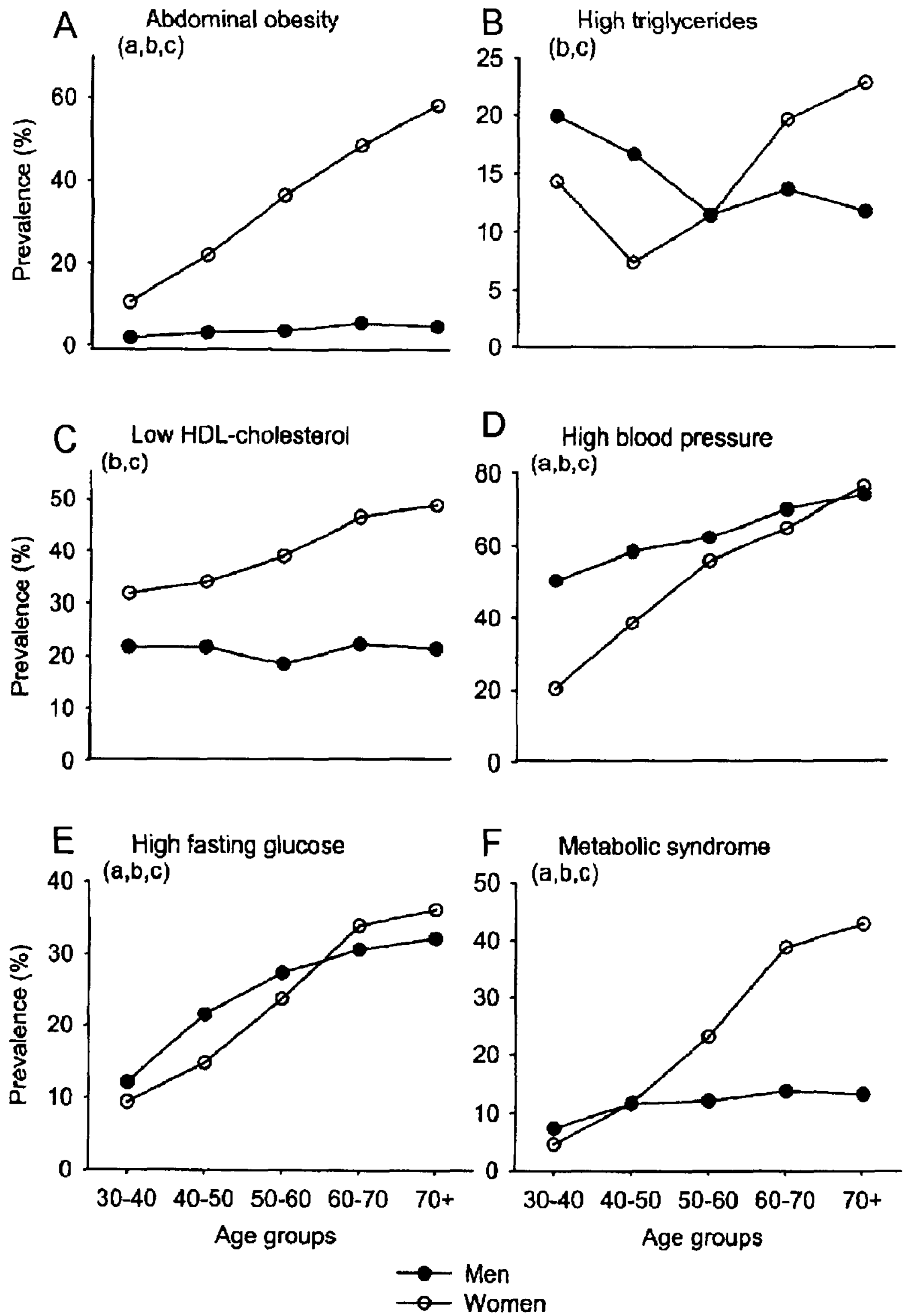

Figure 1. *A) Prevalence of abdominal obesity (ATP III criteria, waist circumference: men > 102 cm; women > 88 cm) by age and sex. B) Prevalence of high triglycerides by age and sex. C) Prevalence of high-density lipoprotein cholesterol by age and sex. D) Prevalence of high blood pressure by age and sex. E) Prevalence of high fasting glucose by age and sex. F) Prevalence of metabolic syndrome by age and sex. Indication: significant trend for men (a); Indication: significant trend for women (b); and Indication: significant interaction between men and women for the trends (c).*

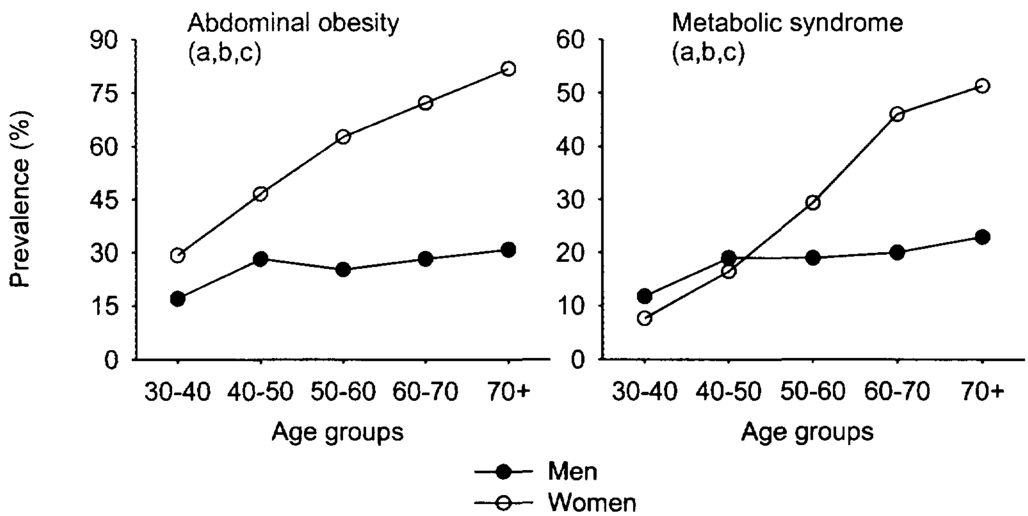

Figure 2. A) Prevalence of abdominal obesity (Asian criteria: waist circumference > 90 cm for men and > 80 cm for women) by age and sex. B) Prevalence of metabolic syndrome (Asian criteria for abdominal obesity) by age and sex. Indication: significant trend for men (a); Indication: significant trend for women (b); and Indication: significant interaction between men and women for the trends (c).

obesity (Figure 2A) and metabolic syndrome (Figure 2B) by age were similar to those defined by ATP III criteria.

DISCUSSION

This is the first report of the prevalence of metabolic syndrome in Chinese based on published criteria from the ATP III. We found that the prevalence of metabolic syndrome increased with age in both men and women. In addition, women had a higher prevalence of metabolic syndrome than men did. Even when cut-off values for defining abdominal obesity for Asian population were used ,a similar gender difference in the prevalence of metabolic syndrome still existed. This gender difference was probably due to the higher prevalence of abdominal obesity and low high-density lipoprotein cholesterol in women than in men.

The prevalence of the metabolic syndrome has been hard to define or compare because of the lack of accepted criteria for the definition of the syndrome.[16,23-25] The European Group for the study of Insulin Resistance database of approximately 1,500 normal Caucasians from 21 clinical centers all over Europe participating in the hyperinsulinemic, euglycemic clamp studies reported a prevalence of 15.6%, according to the World Health Organization definition of the metabolic syndrome.[26] In the rural and urban Palestinian West Bank community, the age-adjusted prevalence of the metabolic syndrome as defined by the World Health Organization was 17%. We are unaware of any report of the prevalence of the metabolic syndrome based on the ATP III criteria. The prevalence of metabolic syndrome in Kinmen was 15.2%, which is close to the estimates in other populations using the World Health Organization criteria. However, the comparability of the World Health Organization and ATP III criteria remains to be investigated.

Insulin resistance related metabolic syndrome is an emerging new risk factor in the Asian populations, but its real impact on prevalence of coronary heart disease remains unclear.[27] In Taiwan, several population,-ased studies have established the relationship between hyperinsulinemia and the conventional atherosclerotic risk factors,[28-30] implying a role for insulin resistance in the development of cardiovascular disease in this region. Specifically, a strong association between hyperinsulinemia and obesity has consistently been recognized in adults[28, 31] and children.[32] The present study further demonstrated that the real burden of metabolic syndrome might depend critically on the definition of abdominal obesity. When the Asian criteria for abdominal obesity were adopted, the prevalence of the metabolic syndrome increased dramatically from 15.42% to 21.16% for the population of Kinmen.

The definition of metabolic syndrome based purely on clinical risk factors without referring to direct indices of insulin resistance may be supported by the high prevalence of insulin resistance in subjects with the clinical risk factors.[33] Bonora et al reported that the prevalence of insulin resistance was 65.9% in subjects with impaired glucose tolerance, 83.9% in subjects with type II diabetes, 53.5% in hypercholesterolemia subjects, 84.2% in hypertriglyceridemia subjects, 88.1% in subjects with low high-density lipoprotein cholesterol, 62.8% in hyperuricemia subjects, and 58.0% in hypertension subjects.[33] The prevalence of insulin resistance in subjects with the combination of glucose intolerance (impaired glucose tolerance or type II diabetes), dyslipidemia (hypercholesterolemia and/or hypertriglyceridemia and/or low high-density lipoprotein cholesterol), hyperuricemia, and hypertension was 95.2%. In isolated hypercholesterolemia, hypertension, or hyperuricemia, prevalence rates of insulin resistance were not higher than that in nonobese, normal subjects. An appreciable number of subjects (9.6% of the population) were insulin resistant but free of impaired glucose tolerance, type II diabetes, dyslipidemia, hyperuricemia, and hypertension. These results from a population-based study documented that the vast majority of subjects with multiple metabolic disorders were insulin resistant.

Previous studies have shown that women display enhanced insulin sensitivity compared to men even after adjustment for percent body fat.[34-37] The gender difference in insulin resistance is consistent with the established observation that mortality rate from coronary heart disease is much higher among men than women (except in diabetes mellitus) and may suggest that hyperinsulinemia/insulin resistance may partly underlie such a difference.[35, 37] In insulin resistance-related metabolic syndrome, gender-specific differences have been reported.[38] Gender differences in the relationships between hyperinsulinemia and other potential components of metabolic syndrome have also been observed in Chinese in Taiwan.[28, 31, 39, 40] In the present study, women had a higher prevalence of metabolic syndrome than men in Kinmen. The result appears to be contradictory to the relationship between metabolic syndrome and the risk of coronary artery disease.[18] One reason for the unexpectedly high prevalence of the metabolic syndrome in women in Kinmen may be that the ATP III criteria are inappropriate for Chinese people.[41] On the other hand, the observed disadvantageous risk factor profile in women may be a true warning sign that should alert our public health policy makers to the need for preventive interventions in Kinmen. Further studies of long-term follow-up or the analysis of mortality patterns between men and women may be useful in clarifying this important issue.

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以臨床準則估計金門線代謝異常症候群之盛行率

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背景：代謝異常症候群對全世界的心血管疾病所產生的負擔十分重要。本研究根據第三次國際膽固醇教育計劃（ATP III）所訂定的代謝異常症候群之臨床定義，來估計金門地區的代謝異常症候群之盛行率。

方法：我們分析 8320 位年齡介於 30–92 歲曾參與社區橫段性研究的民眾資料，根據 ATP III 所訂定的代謝異常症候群之臨床定義，只要同時存在 3 種或大於 3 種下列危險因子，即定義爲代謝異常症候群；中廣型肥胖（腰圍：男性>102 公分；女性>88 公分）、偏高的三酸甘油酯（≥150 毫克/公合）、偏高的血壓（≥130/≥85 毫米汞柱）、偏低的高密度脂蛋白膽固醇（男性<40 毫克/公合；女性<50 毫克/公合）、偏高的空腹血糖（≥110 毫克/公合）。

結果：女性的代謝異常症候群盛行率（878/4,716;18.62%）明顯高於男性（405/3,604;11.24%，$p<0.001$）。各項組成代謝異常症候群之危險因子的男女盛行率分別爲：中廣型肥胖爲 3.72% 與 28.52%（$p<0.001$）、偏高的三酸甘油酯爲 13.37% 與 10.45%（$p<0.001$）、偏低的高密度脂蛋白膽固醇爲 20.98% 與 37.66%（$p<0.001$）、偏高的血壓爲 61.07% 與 43.74%（$p<0.001$），以及偏高的空腹血糖爲 23.25% 與 19.64%（$p<0.001$）。當中廣型肥胖定義爲男性腰圍 90 公分與女性 80 公分時，代謝異常症候群的盛行率女性仍然顯著高於男性（23.77% *vs* 17.73%, $p<0.001$）。

結論：金門地區代謝異常症候群的盛行率有顯著的性別差異，可能是女性有較高的中廣型肥胖與偏低的高密度脂蛋白膽固醇盛行率。

關鍵詞：胰島素阻抗；代謝異常症候群；族群研究。

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Metabolic Syndrome — An Important but Complex Disease Entity for Asians

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The significance of metabolic syndrome has gradually become unraveled in recent years. In the past, hypercholesterolemia and cholesterol metabolism were the focus of atherosclerotic disease studies, while findings from Taiwan and other Asian countries often indicated that hypertriglyceridemia coupled with low high-density lipoprotein cholesterol (HDL-C) was associated with coronary heart diseases to a greater extent than hypercholesterolemia.[1] However, the independent role of hypertriglyceridemia was not recognized as important until the 1990s, when evidence was obtained from studies on non-insulin-dependent diabetes mellitus (NIDDM) patients and post-menopausal women.[2] The post-prandial triglyceride (TG) level has been deemed more important than that of the fasting state.[3] This recent recognition may be due to a rapid increase in obesity prevalence around the world and the success in curbing hypercholesterolemia in western countries, which have diverted our research focus. We now know that the association between hypertriglyceridemia and cardiovascular (CV) diseases in Chinese and other Asian populations is an integral part of the multiple metabolic syndrome.

The metabolic syndrome is a condition characterized by a constellation of obesity-related and CV disorders. It was first termed "X syndrome" by Kylin in the 1920s, described as a phenomenon of the clustering of obesity, hypertension and gout.[4] The concept of syndrome X was reintroduced by Reaven in the late 1980s for the clustering of CV risk factors, including hypertension, insulin resistance/hyperinsulinemia/glucose intolerance, elevated very-low-density lipoprotein TG, and low HDL-C concentrations.[5] Many of his initial clinical studies were carried out in Taiwan,[6, 7] where the impact of metabolic syndrome is particularly strong, as it is in many other East- and South-Asian and non-Caucasian populations. As early as the 1980s, comparative studies between South Asians and Caucasians living in the UK began being published. These studies indicated that the prevalence of coronary artery disease in patients of South-Asian origin cannot be explained on the basis of elevated serum cholesterol or fibrinogen, smoking or hypertension.[8] Low plasma HDL-C, high plasma TG and insulin levels, and a high prevalence of NIDDM have been consistently found among South Asians living overseas. African Americans and Hispanics also seem to be more insulin resistant than non-Hispanic whites.[9]

Table 1. Criteria used in defining the metabolic syndrome proposed by WHO

Component	Description of Criteria
Dyslipidemia	Elevated plasma triglyceride (≥ 1.7 mmol/L) and/or low HDL-cholesterol concentrations (< 0.9 mmol/L for men; < 1.0 mmol/L for women)
Obesity	BMI = 30kg/m^2 and/or high waist-to-hip ratio (> 0.9 for men; > 0.85 for women)
Hypertension	Antihypertensive treatment or high blood pressure (> 160/90 mmHg)
Microalbuminuria	Overnight urinary albumin excretion rate ≥ 20 μg/min

Table 2. Criteria used in defining the metabolic syndrome in NCEP-ATP III

Risk Factor	Diagnostic Criteria
Abdominal obesity	Waist circumference > 102 cm for men; > 88 cm for women
Triglyceride	≥ 150 mg/dL
HDL-cholesterol	< 40 mg/dL for men; < 50 mg/dL for women
Blood pressure	≥ 130/85 mmHg
Fasting glucose	≥ 110 mg/dL

It is timely to study the significance of metabolic syndrome in Taiwan. The work by Chuang et al in the accompanying article used a modified National Cholesterol Education Program – Adult Treatment Panel (NCEP–ATP) III definition, which should draw our attention to the complexity and meaning of metabolic syndrome across ethnic groups. A unifying definition of the syndrome was first proposed in "*Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation*" in 1998.[10] According to this definition, a person with type II DM or impaired glucose tolerance has the metabolic syndrome if at least two of the component criteria are satisfied. The components involved include dyslipidemia (elevated plasma TG or low HDL-C), obesity (large body mass index [BMI] or waist-to-hip ratio), hypertension and microalbuminuria. Even with normal glucose tolerance, a person with insulin resistance is also considered to have the metabolic syndrome if at least two of the criteria are satisfied.

On the other hand, the criteria suggested by the NCEP-ATP III guidelines primarily used readily available CV risk factors — fasting plasma TG, HDL-C, glucose and blood pressure (BP) — whose cut-off points were lowered to a high normal range.[11] In addition, waist circumference was used to define obesity, focusing on abdominal adiposity. A person is diagnosed as having the metabolic syndrome if three or more of the criteria are satisfied.

The definition used in the World Health Organization (WHO) diabetes report centers on diabetes and insulin resistance, but the NCEP-ATP III guidelines give equal weights to abdominal adiposity, hypertension, hyperglycemia, hypertriglyceridemia and low HDL-C. While both of these definitions are useful in identifying patients with metabolic disorders who need clinical attention, the prevalence rate estimates based on these two definitions will not be comparable. Even for a given definition, it is also likely that the prevalence and the combination patterns of the metabolic components vary across populations and across gender groups, and thus will not be comparable.

When we used data from the Nutrition and Health Survey in Taiwan (NAHSIT)[12] and the US National Health and Nutrition Examination Survey III (NHANES III) (Figure) to estimate the prevalence rate of the metabolic syndrome following the NCEP-ATP III guidelines, the clustering of high BP, TG and HDL-C with or without large waist circumference was most common for Taiwanese men, while the US non-Hispanic white population showed a more evenly distributed pattern. Most Taiwanese women had a clustering of high HDL-C, BP and waist circumference, while most white women had a syndrome of high HDL-C, TG, and waist circumference. Abdominal obesity seems more prevalent for women than for men across populations. The meaning of these different combination patterns should be carefully delineated.

The difference between the WHO and NCEP definitions of the metabolic syndrome have fueled the controversy as to its underlying cause. Several hypotheses regarding the etiology of the multiple metabolic syndrome have been postulated in the literature.[13] The insulin resistance/hyperinsulinemia hypothesis was the basis of the definition adopted in the WHO DM report, which attributes the cooccurrence of disorders to primary insulin resistance. Another hypothesis is that central adiposity is the underlying cause of multiple metabolic and hemodynamic disturbances; however, only part of them is mediated by insulin-related metabolism. In addition, the lipotoxicity hypothesis states that the metabolic syndrome and type 2 diabetes can be caused by the accumulation of TGs and long-chain fatty-acyl-CoA in the liver, muscle and islet.[14] Given the complexity and uncertainty in the underlying cause of the metabolic syndrome, the NCEP–ATP III definition lies in the middle, applying only the concept of clustering without favoring any component facet.

The complexity broadens when defining the metabolic syndrome across ethnic groups. The cut-off points for abdominal obesity (waist circumference 102 cm for men; 88 cm for women) used in the NCEP-ATP III guidelines were designed for Caucasians. Editors and reviewers have suggested that the Kinmen study should apply cut-off points that are suitable for Taiwanese. Waist circumferences of > 90 cm for males and > 80 cm for females were adopted since these are the cut-off points suggested by the International Obesity Task Force, a non-profit organization that works closely with WHO and uses Japanese data. The same cut-off points were also recently selected to define abdominal obesity in Taiwan, since data from the Nutrition

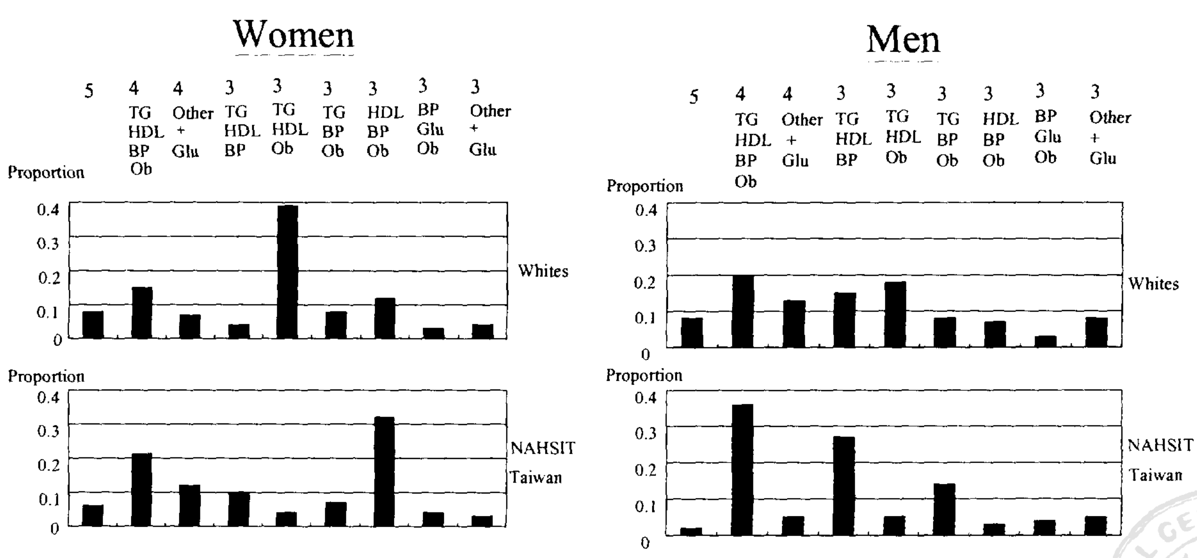

Figure *Patterns of multiple metabolic syndrome in Taiwanese and in US non-Hispanic whites (TG = high triglyceride; HDL = low HDL-cholesterol; BP = high blood pressure; Ob = large waist circumference).*

and Health Survey in Taiwan (1993–1996) showed that the mean waist circumferences for men and women whose BMI is in the range of 27 are approximately 90 cm and 80 cm, respectively. The BMI value of 27 has been adopted as the cut-off point for general obesity in Taiwanese.

The impact of metabolic syndrome is likely to be substantial in Taiwan, given the low mean BMI (observed in various Taiwanese surveys) but high incidence rate of DM.[15] Our recent study has demonstrated that the risk of increasing BMI for hypertension, diabetes and hypertriglyceridemia is greater for Taiwanese than for non-Hispanic American whites.[16] This suggests that future research should address the significance of the metabolic syndrome in CV incidence, including stroke, coronary artery diseases and peripheral artery diseases.

A large body of evidence has accumulated, showing that the multiple metabolic syndrome may play an important role in the etiology of CV diseases. However, the evidence pertains primarily to each individual component disorder separately. In order to study the impact of metabolic syndrome per se, a natural history of the syndrome should be clearly delineated. Longitudinal studies are needed to document the sequences of component metabolic disorders.[13] Overall, the multiple metabolic syndrome has caught the attention of health professionals around the world. The major challenge ahead is to understand its pathogenesis and to identify effective measures to prevent the clustered events of obesity and multiple metabolic disorders.

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