Can We Apply the National Cholesterol Education Program Adult Treatment Panel Definition of the Metabolic Syndrome to Asians?

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OBJECTIVE — Limited information is available about the metabolic syndrome in Asians. Furthermore, the definition of central obesity using waist circumference may not be appropriate for Asians. The objectives of this study were to determine the optimal waist circumference for diagnosing central obesity in Asians and to estimate the prevalence of the metabolic syndrome in an Asian population.

RESEARCH DESIGN AND METHODS — We used data from the 1998 Singapore National Health Survey, a cross-sectional survey involving 4,723 men and women of Chinese, Malay, and Asian-Indian ethnicity aged 18–69 years. Receiver operating characteristic analysis suggested that waist circumference >80 cm in women and >90 cm in men was a more appropriate definition of central obesity in this population. The prevalence of the metabolic syndrome was then determined using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria with and without the modified waist circumference criteria.

RESULTS — In Asians, decreasing waist circumference increased the crude prevalence of the metabolic syndrome from 12.2 to 17.9%. Using the modified Asian criteria, the prevalence of the metabolic syndrome increased from 2.9% in those aged 18–30 years to 31.0% in those aged 60–69 years. It was more common in men (prevalence 20.9% in men versus 15.5% in women; $P < 0.001$) and Asian Indians (prevalence 28.8% in Asian-Indians, 24.2% in Malays, and 14.8% in Chinese; $P < 0.001$).

CONCLUSIONS — NCEP ATP III criteria, applied to an Asian population, will underestimate the population at risk. With a lower waist circumference cutoff, the prevalence of the metabolic syndrome is comparable to that in Western populations. Ethnic differences are likely to exist between populations across Asia.

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The metabolic syndrome represents a constellation of metabolic derangement including central obesity, glucose intolerance, hyperinsulinemia, low HDL cholesterol, high triglycerides, and hypertension (1). Subjects with the metabolic syndrome are at increased risk for diabetes (2) and cardiovascular disease (CVD) (3). The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) report (4) recommended the use of five variables for diagnosis of the metabolic syndrome, including waist circumference, serum triglyceride level, serum HDL cholesterol level, blood pressure, and fasting glucose level. Subjects meeting three of these five criteria were classified as having the metabolic syndrome. On the basis of this definition, the Third National Health and Nutrition Examination Survey (NHANES III) reported that the age-adjusted prevalence of the metabolic syndrome in the U.S. was 23.7%; the highest prevalence was found among Mexican Americans (5).

The World Health Organization (WHO) criteria for diagnosis of the metabolic syndrome (6) is more complex because it takes into consideration microalbuminuria, plasma insulin level, and BMI (instead of waist circumference). Due to the lack of standardization and the unavailability of assays for insulin and microalbuminuria in Asia, use of the NCEP ATP III criteria is preferred because they can be easily applied to the primary care setting in many parts of Asia.

To fully assess the public health implications of the metabolic syndrome in Asia, two important issues concerning the metabolic syndrome must be addressed. First, there is some concern that the recommended cutoff for waist circumference in the NCEP ATP III definition is inappropriate for an Asian population such as ours due to the smaller build of the population (7–10). Data from Singapore had previously demonstrated that for any given percentage of body fat, BMI of Singaporeans was 3 kg/m^2 lower than that in Caucasians (11). A review of other Asian data also concluded that Asians had a higher percentage body fat at a lower BMI compared with Caucasians (12–14). Furthermore, subjects of Chinese descent have been shown to have similar risk of glucose intolerance at lower BMI compared with indigenous Europeans (15). It seems likely that these findings involving BMI would also apply to other anthropometric indexes such as waist circumference.

Second, studies in the U.S. have shown ethnic variation in the prevalence

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of the metabolic syndrome (5,16,17). It is higher in Mexican Americans and Native Americans. The prevalence of the metabolic syndrome in ethnic groups residing in Asia is largely unknown. This becomes especially pertinent given that Asia is the region in which the prevalence diabetes and CVD are likely to see the largest increases in the near future.

The aims of this study were *1*) to determine the optimal definition for the metabolic syndrome in Asians, particularly in relation to waist circumference, and 2) to determine the prevalence of the metabolic syndrome in Chinese, Malays, and Asian Indians living in a highly urbanized environment within Asia. We believe that the prevalence of the metabolic syndrome in the three ethnic groups in Singapore would provide a glimpse of the scope of current and potential problems in Asia as other countries undergo economic transition and rapid urbanization.

RESEARCH DESIGN AND METHODS

— The National Health Survey 1998 was an initiative to determine the risk factors for the major noncommunicable diseases in Singapore such as diabetes, coronary heart disease, stroke, and hypertension. The protocols and procedures used in the National Health Survey 1998 have been reported previously (18) and were based on the WHO-recommended model for field surveys of diabetes and other noncommunicable diseases and the WHO MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) protocol for population surveys. The study was conducted by the Ministry of Health, Singapore. Informed consent was obtained from all participants in the survey.

The survey was conducted at six selected centers throughout Singapore. Systematic sampling according to household types, followed by disproportionate stratified sampling by ethnic groups, was used to select the sample for the survey. The two minority groups, Malays and Asian Indians, were oversampled to give an ethnic distribution of 64% Chinese, 21% Malays, and 15% Asian Indians to ensure sufficient numbers for statistical analysis. A total of 4,723 subjects were finally studied. Data recorded included waist circumference, waist-to-hip ratio, BMI, and blood pressure, glucose, insulin, and lipid levels.

Total cholesterol (intra-assay coefficient of variation [CV] 0.8%, interassay CV 1.7%), triglycerides (intra-assay CV 1.5%, interassay CV 1.8%), and glucose (intra-assay CV 0.9%, interassay CV 1.8%) were measured using a BM/Hitachi 747/737 analyzer (Hitachi) using the enzymatic calorimetric method. HDL cholesterol (intra-assay CV 2.9%, interassay CV 3.6%) was measured using a homogenous calorimetric assay, whereas LDL cholesterol (intra-assay CV 0.9%, interassay CV 2.0%) was measured using a homogenous turbidimetric assay. Waist circumference was measured at the narrowest part of the body below the costal margin, and hip circumference was measured at the widest part of the body below the waist. Fasting blood specimens for lipids, insulin (10-ml plain tubes), and glucose (2-ml fluoride oxalate tubes) were collected from all respondents after a 10-h overnight fast. All subjects except those being treated for diabetes then underwent an oral glucose tolerance test (75 g anhydrous glucose made up to 250 ml of solution with water).

Definition of the metabolic syndrome

The metabolic syndrome was diagnosed according to the NCEP ATP III definition. A participant was deemed to have the metabolic syndrome when three or more of the following criteria were satisfied: *1*) waist circumference >102 cm in men and >88 cm in women; *2*) triglyceride level ≥1.7 mmol/l; *3*) HDL cholesterol <1.0 mmol/l in men and <1.3 mmol/l in women; 4) blood pressure ≥130/85 mmHg or known treatment for hypertension; and *5*) fasting glucose level of ≥6.1 mmol/l or known treatment for diabetes.

The NCEP ATP III criteria were ambiguous about subjects known to have hypertension and diabetes, especially those being treated for those conditions. Therefore, we opted to treat both categories of subjects in the following manner. Subjects being treated for hypertension could have blood pressure below the predefined cutoff, but we considered these subjects as having blood pressure ≥130/85 mmHg. Similarly, subjects being treated for diabetes, regardless of the fasting glucose level, were considered as having fasting glucose ≥6.1 mmol/l. However, they were not considered as having the metabolic syndrome unless they had fulfilled at least three criteria.

Statistical analysis

Receiver operating characteristic (ROC) analysis was used to identify the optimal cutoff of waist circumference as a predictor of the presence of at least two other features of the metabolic syndrome. Waist circumference of 84.4 cm was most sensitive and specific in men, whereas in women it was 75.9 cm (data not shown).

However, features such as blood pressure and triglycerides show greater intra-individual variation than glucose and HDL cholesterol. Therefore, we also used ROC analysis to identify the level of waist circumference that best predicted the clustering of impaired glucose metabolism (fasting hyperglycemia or diabetes) and HDL cholesterol, because both of these parameters are more robust and less susceptible to variations. Even then, the waist circumference that best predicts a clustering of impaired glucose metabolism and low HDL cholesterol was 89.2 and 78.9 cm in men and women, respectively (data not shown). This was significantly less than the cutoff recommended by the NCEP ATP III of 102 and 88 cm in men and women, respectively.

This figure was close to the cutoff recommended in the report by the International Diabetes Institute/Western Pacific World Health Organization/International Association for the study of Obesity/International Obesity Task Force (19). For this reason, we used a waist circumference cutoff of >90 and >80 cm in men and women, respectively, for the modified Asian criteria. We calculated the prevalence of the metabolic syndrome by age group, sex, and ethnic group, using both sets of criteria.

To ensure that the survey findings were representative of the Singapore population, the prevalence was weighted to the Singapore 1998 population estimates to correct for the different age, sex, and ethnic distribution between the survey sample and the population due to oversampling of the minority ethnic groups. All analyses were performed with the STATA statistical software (version 6.0; Stata, College Station, TX), except the ROC analysis, which was conducted using SPSS (version 11; SPSS, Chicago, IL).

RESULTS

— The prevalence of central obesity in men and women across ethnic groups is shown in Table 1. There was greater prevalence of central obesity in Asian Indians compared with Chinese or

Table 1—*Prevalence* of central obesity by ethnic group and sex*

	NCEP ATP III waist circumference†		Asian waist circumference‡	
	Men	Women	Men	Women
Ethnic group				
Chinese	3.7 (3.0–4.7)	6.9 (5.9–8.2)	26.2 (24.2–18.2)	21.0 (19.3–23.0)
Malay	4.8 (2.9–7.8)	22.0 (17.6–27.0)	29.8 (24.9–35.2)	43.2 (37.7–48.9)
Indian	8.6 (5.3–13.6)	25.5 (19.5–32.6)	41.4 (34.5–48.7)	53.8 (46.2–61.2)

Data are % (95% CI). *Prevalence standardized to 1998 Singapore population, weighted for age, sex, and ethnic distribution; †NCEP ATP III waist circumference cutoffs: >102 cm in men, >88 cm in women; ‡Asian waist circumference cutoffs: >90 cm in men, >80 cm in women.

Malays using either NCEP ATP III criteria or the modified Asian criteria. With the modified criteria, the prevalence of central obesity increased in all three ethnic groups, especially in Asian-Indians and Malays.

The crude prevalence of the metabolic syndrome in our population using the NCEP ATP III criteria was 12.2% (95% CI 11.3–13.2). Using modified Asian criteria with a lower cutoff for waist circumference, the crude prevalence of the metabolic syndrome in Singapore was 17.9% (16.8–19.0).

The prevalence of the metabolic syndrome in Singapore, stratified by ethnic group and sex, is shown in Table 2. In men, prevalence of the metabolic syndrome using the NCEP ATP III criteria was 13.1% but increased to 20.9% with the modified Asian criteria. Similarly, the prevalence in women using NCEP ATP III criteria was 11.0% and increased to 15.5% with the modified Asian criteria.

The prevalence of the metabolic syndrome in men was significantly higher than in women with both the NCEP ATP III criteria and the Asian criteria. Furthermore, significant differences in the prevalence of the metabolic syndrome were noted between ethnic groups. Using the modified Asian criteria, the age-adjusted prevalence rates in the three ethnic groups were 28.8, 24.2, and 14.8% for Asian Indians, Malays, and Chinese, respectively (Table 2). The differences between Chinese and the other two ethnic group were highly significant ($P < 0.001$).

The prevalence of the metabolic syndrome increased with age, from 2.9% in those aged 18–30 years to 31.0% in those aged 60–69 years (Table 2). In those aged ≥40 years, 28.6% (26.7–30.6) satisfied the Asian criteria for the metabolic syndrome. The increasing prevalence with age was seen across all three ethnic groups. However, the prevalence was higher in the Malays and Asian Indians compared with the Chinese across each age-group.

Using the NCEP ATP III criteria, the age-adjusted prevalence of the metabolic syndrome was 39.9% in individuals with impaired glucose tolerance (IGT), 59.7% in those with newly diagnosed diabetes, and 57.8% in patients with known diabetes. With the Asian criteria, the prevalence increased to 49.6, 74.3, and 73.2%, respectively, in these groups.

CONCLUSIONS — Using the original NCEP ATP III criteria, the crude prevalence of the metabolic syndrome in Singapore was 12.2% and considerably lower than the crude prevalence of 21.8% reported in the U.S. (NHANES III) (5). This was surprising considering the very high prevalence of diabetes (20,21) in this region. Furthermore, CVD mortality and morbidity rates in Singapore are higher than those in the U.S. and seem to be related to the high prevalence of the various features of the metabolic syndrome in our population. For example, Asian Indians, who have the highest risk of CVD mortality and morbidity in our population, have the highest prevalence of diabetes and the lowest HDL cholesterol levels (20).

We believe that the NCEP ATP III definition of the metabolic syndrome, when applied to an Asian population, underestimates the prevalence of the metabolic syndrome and fails to identify many individuals at risk for future CVD. The greatest discrepancy is likely to lie in the definition of central obesity using the waist circumference. Local and regional data have shown that the same level of BMI connotes a greater degree of obesity in Asians compared with Caucasians (11–14) and that Asians are prone to disorders such as diabetes, hypertension, and dyslipidemia at lower levels of BMI than in Caucasian populations (7,9,10,22). With the NCEP ATP III definition of central obesity (>102 cm in men and >88 cm in women), <10% of the men across all three ethnic groups would have been classified as having central obesity (Table 1). Similarly, only 22% of the Malay women and 25.5% of Asian-Indian women would have been classified as having central obesity. Considering the higher prevalence of diabetes (20) and coronary artery disease (23) in these two ethnic groups, it was inconceivable that only a minority would be classified as having central obesity, a well-known feature of the metabolic syndrome. Further support for a lower waist circumference cutoff came from the observation that only half of the diabetes population would have been labeled as having the metabolic syndrome with the original NCEP ATP III criteria. Because

Table 2—*Prevalence* of the metabolic syndrome by ethnic group and sex*

	Original NCEP ATP III criteria		
	Men	Women	Total
Ethnic group			
Chinese	10.8 (9.5–12.3)	8.3 (7.2–9.6)	9.4 (8.5–10.4)
Malay	17.3 (13.5–22.0)	20.0 (15.8–24.9)	18.7 (15.8–22.0)†
Indian	21.7 (16.4–28.3)	19.3 (14.0–26.0)	20.4 (16.5–25.0)†
All races	13.1 (11.8–14.6)	11.0 (9.7–12.3)‡	12.1 (10.8–13.5)
Modified Asian criteria‖			
Chinese	18.1 (16.4–19.9)	12.5 (11.1–14.0)	14.8 (13.7–16.0)
Malay	24.7 (20.2–29.9)	23.8 (19.3–28.9)	24.2 (21.0–27.8)†
Indian	32.4 (26.0–39.5)	25.8 (19.7–33.0)	28.8 (24.3–33.9)†
All races	20.9 (19.3–22.7)	15.5 (14.1–17.1)§	18.2 (16.7–19.9)

Data are % (95% CI). *Prevalence standardized to 1998 Singapore population; †$P < 0.001$ for difference between one ethnic group and Chinese; ‡$P = 0.046$ for difference between two sexes; §$P < 0.001$ for difference between two sexes; ‖waist circumference >90 cm in men and >80 cm in women.

Table 3—*Prevalence* with 95% CI of metabolic syndrome according to modified Asian criteria by ethnic group and age-group*

	18–29 years	30–39 years	40–49 years	50–59 years	60–69 years
Ethnic group					
Chinese	2.1 (1.4–3.2)	4.5 (3.4–6.0)	10.7 (8.9–12.8)	22.1 (18.8–25.9)	25.0 (20.5–30.2)
Malay	8.6 (5.2–14.0)	13.3 (9.2–18.8)	24.5 (18.0–32.5)	35.1 (24.3–47.7)	38.0 (25.2–52.8)
Indian	4.3 (1.6–10.9)	14.6 (9.1–22.6)	26.5 (17.9–37.2)	38.2 (24.9–53.6)	50.8 (33.6–67.7)
All races	2.9 (2.1–4.1)	6.3 (5.1–7.9)	14.9 (12.8–17.3)	26.7 (23.1–30.7)	31.0 (26.2–36.2)

Data are % (95% CI). *Prevalence standardized to 1998 Singapore population.

central obesity is a major feature of the metabolic syndrome, it was important to ascertain what would be an appropriate cutoff in an Asian population.

Our data, from a population comprising three ethnic groups residing in Asia, suggests that waist circumference of 80 cm in women and 90 cm in men represents a more appropriate cutoff for the definition of central obesity in the diagnosis of the metabolic syndrome in Asians. This concurs with the recommendations of the WHO expert consultation, which suggested that appropriate waist circumference should be based on population-specific data and consideration (24). Using these modified criteria, approximately half of subjects with IGT and three quarters of subjects with diabetes (whether new or known) were classified as having the metabolic syndrome. These figures were comparable with the findings of insulin resistance in 65.9 and 83.9% of subjects with IGT and diabetes, respectively (25).

With a lower cutoff for waist circumference, the prevalence of the metabolic syndrome in our population was 17.9%. We believe that this is a better reflection of the true prevalence of the metabolic syndrome in Singapore. Data from Taiwan and Korea had also reported low prevalence of the metabolic syndrome according to the NCEP ATP III criteria, 15.42 (26) and 6.8% (27), respectively, which increased to 21.16% in Taiwanese and 10.9% in Koreans with similar modification to the waist circumference cutoff.

The prevalence of the metabolic syndrome was highest in the Asian Indians (28.8%), followed by the Malays (24.2%), and then the Chinese (14.8%). Differences in prevalence of the metabolic syndrome between Chinese and the other two ethnic groups were seen in both men and women (Table 2). Ethnic differences in prevalence of diabetes or the metabolic syndrome are not unique to Singapore, as it had been demonstrated in several western populations. The Australian Aborigines (28), American Hispanics (16,29), and migrant Indians (30) have all been shown to have higher prevalence of diabetes or the metabolic syndrome. However, most of these minority ethnic groups have social and lifestyle factors that differ considerably from the Europoid population within their respective countries. What is unique about Singapore is that all three ethnic groups live in a fairly homogenous, urbanized environment. Therefore, the difference in prevalence of the metabolic syndrome between ethnic groups is unlikely to be due solely to environmental factors.

The impact of decreasing the waist circumference criteria on the prevalence the metabolic syndrome also differed between ethnic groups. With a lower waist circumference cutoff, the prevalence of the metabolic syndrome increased by 5.4% in Chinese, 5.5% in Malays, and 8.4% in Asian Indians. Two factors contribute to the greater increase in Asian Indians. Firstly, Asian Indians are more centrally obese than Chinese and Malays (20,31). As such, decreasing the waist circumference criteria resulted in the reclassification of a greater number of Asian Indians than Malays and Chinese (Table 1). However, central obesity alone is insufficient to diagnose the metabolic syndrome. The greater increase in the prevalence of the metabolic syndrome in Asian Indians, when the waist circumference criteria was decreased, implied that other features of the metabolic syndrome must also be more common in Asian Indians. It is likely that these were diabetes and low HDL cholesterol level, because both had been shown to be more common in Asian Indians than in Chinese or Malays (20,32).

In line with data from the NHANES III (5), the prevalence of the metabolic syndrome increased with age in all three ethnic groups. It is likely that the young population in Singapore (mean age in 1998 was 34 years) is the reason the crude prevalence of the metabolic syndrome was only 17.9% compared with 23.6% in the U.S. population. As the population demographic changes and our population ages, the impact of the metabolic syndrome will be significantly greater and may even outstrip those in developed countries such as the U.S. This is supported by our data that showed that 28.6% of those aged ≥40 years had features of the metabolic syndrome.

The higher prevalence of the metabolic syndrome at younger ages in Asian Indians and Malays (Table 3) is of particular concern. This means that Malays and Asian Indians will have more prolonged exposure to the proatherosclerotic risk factors associated with the metabolic syndrome. This could explain the previous findings in our population that ethnicity remained a significant predictor of CVD, even after adjustment for diabetes and other CVD risk factors (23). We also know that the presence of the metabolic syndrome precedes the onset of diabetes (33). Prolonged exposure to atherosclerotic risk factors before the onset of diabetes could also contribute to the excess mortality observed in Asian Indians and Malays with diabetes compared with Chinese (34).

In conclusion, decreasing of the criteria for diagnosis of central obesity to a waist circumference of >90 cm in men and >80 cm in women may be more useful in identifying individuals with the metabolic syndrome in Asia. Using these criteria, the prevalence of the metabolic syndrome in Singapore was comparable to that in more developed countries. Some ethnic groups seem more prone to developing the metabolic syndrome. To reduce CVD morbidity and mortality in Asia, lifestyle measures to reduce the prevalence of the metabolic syndrome, through weight reduction and exercise, should play a significant role in future health policies.

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