Should Central Obesity Be an Optional or Essential Component of the Metabolic Syndrome?

Ischemic heart disease risk in the Singapore Cardiovascular Cohort Study

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OBJECTIVE — The International Diabetes Federation (IDF) proposes that central obesity is an "essential" component of the metabolic syndrome, while the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) proposes that central obesity is an "optional" component. This study examines the effect of the metabolic syndrome with and without central obesity in an Asian population with ischemic heart disease (IHD).

RESEARCH DESIGN AND METHODS — From the population-based cohort study (baseline 1992–1995), 4,334 healthy individuals were grouped by the presence or absence of the metabolic syndrome and central obesity and followed up for an average of 9.6 years by linkage with three national registries. Cox's proportional hazards model was used to obtain adjusted hazard ratios (HRs) for risk of a first IHD event.

RESULTS — The prevalence of metabolic syndrome was 17.7% by IDF criteria and 26.2% by AHA/NHLBI criteria using Asian waist circumference cutoff points for central obesity. Asian Indians had higher rates than Chinese and Malays. There were 135 first IHD events. Compared with individuals without metabolic syndrome, those with central obesity/metabolic syndrome and no central obesity/metabolic syndrome were at significantly increased risk of IHD, with adjusted HRs of 2.8 (95% CI 1.8–4.2) and 2.5 (1.5–4.0), respectively.

CONCLUSIONS — Having metabolic syndrome either with or without central obesity confers IHD risk. However, having central obesity as an "optional" rather than "essential" criterion identifies more individuals at risk of IHD in this Asian cohort.

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Recently, two new criteria diagnosing the metabolic syndrome have been proposed, with both allowing three of five components (central obesity, high fasting triglyceride, low HDL cholesterol, hypertension, glucose intolerance). However, the International Diabetes Federation (IDF) proposes that central obesity is an "essential" component (1), while the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) proposes that central obesity is an "optional" component, like the other factors (2). Notably, in particular for Asians, there is agreement for the waist circumference cutoffs between the two criteria. Thus, in Asians, these proposals identify three groups of individuals: *1*) no metabolic syndrome, *2*) central obesity and metabolic syndrome, and *3*) no central obesity and metabolic syndrome (this latter group meets the criteria for metabolic syndrome according to AHA/NHLBI but not IDF). In effect, the IDF criteria identified a subset of Asian individuals who have been identified as having the metabolic syndrome by the AHA/NHLBI criteria.

It has been suggested that the proportion of individuals without central obesity who have three or more components of the metabolic syndrome is small (3,4). It is also felt that in the U.S., for the most part, the same individuals will be identified by either definition so that differences in the definitions are probably insignificant (2). However, this has not been assessed in various populations, particularly in populations comprising ethnic groups from Asia. Furthermore, the impact of central obesity as an essential component of the metabolic syndrome has not been extensively assessed in relation to the risk of ischemic heart disease (IHD). Only one study (5) has shown that the rate of cardiovascular disease (CVD) mortality increased with increasing waist circumference in the presence of two or more other components but not with less than two other components. There have been no such studies in Asian populations. These studies are critical, given that the reason for defining the metabolic syndrome is to provide one practical definition that would be useful for the identification of individuals with increased risk of CVD (6–10) and diabetes (11,12).

The aims of this study are to determine the different prevalence of the metabolic syndrome according to the IDF and AHA/NHLBI definitions and the impact of central obesity as an "essential" rather

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Abbreviations: AHA/NHLBI, American Heart Association/National Heart, Lung, and Blood Institute; AP_E, attributable percent among those with metabolic syndrome; AP_T, attributable percent among the total population; CVD, cardiovascular disease; IDF, International Diabetes Federation; IHD, ischemic heart disease.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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than "optional" component of the metabolic syndrome on the risk of IHD in a healthy Asian population.

RESEARCH DESIGN AND METHODS

— The Singapore Cardiovascular Cohort Study is a population-based prospective study combining two cross-sectional surveys. These are the 1992 National Health Survey (13) and the National University of Singapore Heart Study (1993–1995) (14). The methodologies of these surveys were described in detail and are only briefly described here.

Both surveys were a random sample of all Singapore residents, with disproportionate sampling by ethnic group to increase the number of Malays and Asian Indians relative to Chinese. Consent was obtained from all participants before conduct of study. This study has also been approved by the National University of Singapore institutional review board.

Baseline measurements

Ethnicity was self-reported and classified into Chinese, Malay, or Asian Indian. Two readings of blood pressure were taken after adequate resting using a standard mercury sphygmomanometer. If the two readings differed (diastolic by >15 mmHg or systolic >25 mmHg), a third reading was performed. The mean values of the closest two readings were calculated. Measurements were made of waist circumference (narrowest part of the body below the costal margin), weight, and height. Smoking was categorized as non- or current smoker, and alcohol intake as less than once a month or greater than or equal to once a month. Individuals were asked if they had ever been diagnosed as having preexisting IHD, cerebrovascular disease, diabetes, or hypertension and whether medication was prescribed.

All subjects were examined in the morning following a 10-h fast. Serum total cholesterol, triglyceride, and HDL cholesterol were measured using Kodak Ektachem Clinical Chemistry Slides (Kodak, Rochester, NY), and LDL cholesterol was calculated using the Friedewald formula. Plasma glucose was measured by the glucose oxidase method using blood collected in fluoride oxalate tubes. Individuals with type 2 diabetes were determined from medical history or if the fasting blood glucose was ≥7.0 mmol/l during the physical examination.

Metabolic syndrome criteria

The central obesity/metabolic syndrome status of individuals was obtained using the criteria set out by IDF (1) and AHA/NHLBI (2): *1*) elevated triglycerides: >150 mg/dl (1.7 mmol/l), *2*) reduced HDL cholesterol: <40 mg/dl (1.03 mmol/l) in male subjects and <50 mg/dl (1.29 mmol/l) in female subjects, *3*) elevated blood pressure: systolic ≥130 mmHg or diastolic ≥85 mmHg or on treatment for hypertension, *4*) elevated fasting plasma glucose: ≥100 mg/dl (5.6 mmol/l) or on treatment for type 2 diabetes, and *5*) central obesity, using the waist circumference for South Asians/Asians: ≥90 cm in male subjects and ≥80 cm in female subjects.

Using these five metabolic score components, individuals were categorized into three central obesity/metabolic syndrome groups: *1*) no metabolic syndrome, which includes individuals with less than three metabolic syndrome components; *2*) central obesity and metabolic syndrome, which includes individuals with elevated waist circumference and two or more other components; and *3*) no central obesity and metabolic syndrome, which includes individuals with low waist circumference but three or more other components.

IHD events

Data regarding IHD events were obtained by linking individual records (using unique identity card numbers) to three national registries of the Singapore Ministry of Health: *1*) Registry of Births and Deaths, *2*) Hospital Inpatient Discharge Database (this captures inpatient discharge information from all public and private hospitals, including day-surgery revascularization procedures such as coronary artery angioplasty or coronary stent placement), and *3*) Singapore Myocardial Infarct Registry (this has comprehensive nationwide coverage of acute myocardial infarctions). An IHD event was defined as admission or death due to acute myocardial infarction or IHD (codes 410–414 of the ICD-9). For confidentiality, all personal identifiers were removed from the dataset before analysis.

Data analysis

Statistical analyses were performed using SPSS (version XIII SPSS for Windows, release 13.0.1, 2004; Chicago, IL). Categorical variables were expressed in percentages and continuous variables in means ± SD unless otherwise specified. Incidence rates for first IHD events were calculated for each of the central obesity/metabolic syndrome groups, and Cox proportional hazards regression was used to obtain adjusted hazard ratios (HRs) for first IHD events. The time-to-IHD event was the difference between the date of the first IHD event and the date of entry into the study. Subjects without IHD were censored at 31 December 2002 or the date of non-IHD death, whichever occurred first. HRs were adjusted for age, sex, ethnic group, study, LDL cholesterol, smoking, and alcohol intake. Interaction terms, created using the three central obesity/metabolic syndrome groups, with ethnic group ($P = 0.387$), sex ($P = 0.911$), and study ($P = 0.081$) analyzed separately, showed no significant interaction in the model; thus, the analysis was done with ethnic group, sex, and study combined. An interaction term consisting of follow-up time and the three central obesity/metabolic syndrome groups was used to test the proportional hazards assumption (15) for occurrence of IHD events and was found not to be significant ($P = 0.351$), indicating proportional hazard over time. The attributable percent among those with metabolic syndrome (AP_E: the percent of risk IHD among those with metabolic syndrome that is due to metabolic syndrome) and attributable percent among the total population (AP_T: that is the percent of risk of IHD among the whole population that is due to the metabolic syndrome) was also calculated for both AHA/NHLBI and IDF criteria with and without diabetes.

RESULTS

— There were 4,334 participants after excluding 92 participants with preexisting IHD and 27 with missing data. These comprised 2,546 Chinese, 909 Malays, and 879 Asian Indians. There were 2,087 male subjects and 2,247 female subjects. The mean duration of follow up was 9.6 ± 1.5 years and totaled 41,400 person-years. A total of 135 first IHD events were reported.

Table 1 shows that the prevalence of the three central obesity/metabolic syndrome groups were: no metabolic syndrome, 73.8%; central obesity/metabolic syndrome, 17.7%; and no central obesity/metabolic syndrome, 8.5%. Using the Asian criteria for waist circumference, the prevalence of metabolic syndrome according to the IDF was 17.7% and 26.2% according to the AHA/NHLBI. The prevalence of the three groups was also different among the ethnic groups, with Asian

Table 1—*Characteristics of study population by central obesity/metabolic syndrome groups*

Characteristics	No metabolic syndrome	Central obesity/metabolic syndrome	No central obesity/metabolic syndrome
n (%)	3,200 (73.8)	766 (17.7)	368 (8.5)
Ethnic group*			
Chinese	2,017 (79.2)	309 (12.1)	220 (8.6)
Malays	637 (70.1)	206 (22.7)	66 (7.3)
Asian Indians	546 (62.1)	251 (28.6)	82 (9.3)
Sex*			
Male	1,505 (72.1)	339 (16.2)	243 (11.6)
Female	1,695 (75.4)	427 (19.0)	125 (5.6)
Age (years)†	36.8 ± 11.9	48.8 ± 12.0	47.9 ± 12.2
Total cholesterol (mmol/l)†	5.2 ± 1.0	5.9 ± 1.1	5.8 ± 1.1
LDL cholesterol (mmol/l)†	3.4 ± 0.9	3.9 ± 1.0	3.8 ± 1.4
HDL cholesterol (mmol/l)†	1.3 ± 0.3	1.0 ± 0.3	0.9 ± 0.2
Triglycerides†	1.0	1.9	2.2
Fasting glucose (mmol/l)†	5.3 ± 1.0	6.5 ± 2.4	6.9 ± 2.8
Systolic blood pressure (mmHg)†	114.6 ± 15.2	137.4 ± 21.9	136.3 ± 20.3
Diastolic blood pressure (mmHg)†	67.6 ± 10.9	81.9 ± 11.9	80.9 ± 11.5
Waist circumference (cm)†	73.1 ± 9.4	92.6 ± 8.4	79.8 ± 6.6
BMI (kg/m^2)†	22.1 ± 3.4	29.0 ± 3.8	23.8 ± 2.5
Diabetes†	81 ± 2.5	195 ± 25.5	102 ± 27.7
Current smoker*	580 (18.1)	119 (15.6)	95 (25.8)
Alcohol intake*	316 (9.9)	69 (9.0)	55 (14.9)
Study*			
NHS 92	2,684 (83.9)	434 (56.7)	291 (79.1)
NUHHS	516 (16.1)	332 (43.3)	77 (20.9)

Data are *n* (%) or means ± SD. *Categorical variables; for ethnic group and sex, percentages are shown. †Continuous variables; for triglycerides, median values are shown. NHS 92, 1992 National Heart Study; NUHHS, National University of Singapore Heart Study.

Indians having the highest prevalence of metabolic syndrome in both the presence (28.6%) and absence (9.3%) of central obesity (Table 1).

Table 1 further describes the characteristics of the three central obesity/metabolic syndrome groups. Compared with those with three or more metabolic syndrome components without central obesity, those with three or more components with central obesity were older, more obese, and had higher blood pressure. In addition, they were more likely to be female and of Malay or Asian-Indian ethnicity. However, in contrast, individuals with three or more metabolic syndrome components without central obesity had higher plasma triglyceride and higher fasting glucose values than those with three or more components with central obesity. Also, in this group, there was a higher proportion of current smokers (25.8%) compared with the group with three or more components with central obesity (15.6%) or no metabolic syndrome (18.1%).

Table 2 shows the risk of IHD for the three central obesity/metabolic syndrome groups including and excluding individuals with type 2 diabetes. The highest incidence rates were for the central obesity/metabolic syndrome and no central obesity/metabolic syndrome groups, which included diabetic patients at 8.8 and 9.5 per 1,000 person-years, respectively. Compared with the no metabolic syndrome group, individuals with central obesity/metabolic syndrome and no central obesity/metabolic syndrome had significantly increased risks for IHD with adjusted HRs of 2.8 (95% CI 1.8–4.2) and 2.5 (1.5–4.0), respectively. A comparison of the central obesity/metabolic syndrome and no central obesity/metabolic syndrome groups showed no significant difference in risk of IHD between them, with HR 1.0 (95% CI 0.6–1.5) and an absolute rate difference of 0.7 (−4.7 to +3.2).

The exclusion of diabetic patients did not greatly reduce the risk of IHD for both central obesity/metabolic syndrome or no central obesity/metabolic syndrome groups (adjusted HR 2.5 [95% CI 1.6–4.2] and 1.9 [1.0–3.3], respectively), and there was not a significant difference between the two groups.

Individuals with the metabolic syndrome using either the IDF or AHA/NHLBI criteria were found to have an increased risk of IHD (Table 3). The exclusion of diabetic patients did not remarkably change the risk estimates for either the IDF or AHA/NHLBI criteria and adjusted HRs were similar (HR 2.3 [95% CI 1.5–3.6] using both criteria). The AP_E among those with metabolic syndrome according AHA/NHLBI criteria was higher (84%) than the IDF criteria (76%). Similarly, the AP_T was also found to be higher when the AHA/NHLBI criteria were used (57.6%) compared with the IDF criteria (36.4%). Although the AP_E did not change when diabetic patients were excluded from the analyses, the AP_T was lowered to 48.0 and 28.0% for the AHA/NHLBI and IDF criteria, respectively.

CONCLUSIONS — Our study showed that the prevalence of the metabolic syndrome is 17.7% based on IDF criteria but 26.2% based on AHA/NHLBI criteria. This meant that 8.5% of the population had three or more metabolic syndrome components in the absence of central obesity while using the Asian definition. Thus, making central obesity an "essential" rather than "optional" component in diagnosing metabolic syndrome fails to identify a fairly large proportion of individuals who otherwise would be classed as having the metabolic syndrome.

Our study also showed that individuals in central obesity/metabolic syndrome and no central obesity/metabolic syndrome groups are at similar risk of IHD. This suggests that including central obesity as an "essential" component for the diagnosis of metabolic syndrome, as proposed by IDF, does not add more to the identification of individuals at increased risk of IHD. These findings from our study suggest, at least in this Asian popu-

Table 2—*Association of central obesity/metabolic syndrome groups with risk of IHD*

	n of events (%)	Person-years	Incidence rate (per 1,000 person-years)	HR (95% CI)*	HR (95% CI)†
Including diabetic patients					
No MetS	44 (1.4)	31,318	1.4 (0.9–1.8)	1.0	1.0
CO/MetS	59 (7.7)	6,716	8.8 (6.6–11.0)	6.1 (4.1–9.0)	2.8 (1.8–4.2)
No CO/MetS	32 (8.7)	3,366	9.5 (6.5–13.4)	6.7 (4.2–10.6)	2.5 (1.5–4.0)
CO/ MetS vs. no CO/MetS				0.9 (0.6–1.4)	1.0 (0.6–1.5)
Excluding diabetic patients					
No MetS	40 (1.3)	30,541	1.3 (0.9–1.7)	1.0	1.0
CO/MetS	38 (6.7)	5,013	7.6 (5.2–10.0)	5.6 (3.6–8.8)	2.5 (1.6–4.2)
No CO/MetS	18 (6.8)	2,453	7.3 (4.3–11.5)	5.5 (3.2–9.7)	1.9 (1.0–3.3)
CO/MetS vs. no CO/MetS				1.0 (0.6–1.8)	1.2 (0.8–1.5)

*Unadjusted HRs. †Adjusted HRs for age, study, ethnic group, sex, LDL cholesterol, smoking (nonsmoker vs. current smoker), and alcohol intake (none/occasional vs. ≥1/month). CO, central obesity; MetS, metabolic syndrome.

lation, that having central obesity as an "optional" component of the metabolic syndrome instead of an "essential" component identifies a significantly greater number of individuals at increased risk of IHD. From the absolute measures, the AP_E and AP_T using the AHA/NHLBI criteria was higher than the IDF criteria. Thus, individuals with the metabolic syndrome, using the AHA/NHLBI criteria, can attribute a higher proportion of their risk of IHD to the metabolic syndrome. Similarly, a higher proportion of the risk of IHD for the total study population can be attributed to metabolic syndrome using the AHA/NHLBI rather than the IDF criteria.

The IDF based their recommendation on the strength of the evidence linking waist circumference with CVD and the other components of the metabolic syndrome (16,17) and states that central obesity is an early step in the etiological cascade leading to the full metabolic syndrome. Our findings refute neither of these premises. Indeed, one study (18) in Japan has shown that visceral adiposity was a crucial determinant on the degree of insulin resistance associated with the presence of other metabolic syndrome components. In that study, the presence of three or more metabolic syndrome components was associated with a lesser degree of insulin resistance if visceral adiposity was not one of the three components (versus if it was). However, in relation to identifying individuals at increased risk of IHD, it does appear that central obesity adds to the risk of IHD in much the same way as the other four risk factors. This is in line with the findings of Katzmarzyk et al. (5), who showed that increasing waist circumference was associated with increased risk of CVD mortality when added to the other components of the metabolic syndrome. However, the presence of central obesity as one of the components of metabolic syndrome does not appear to alter the association between the presence of other multiple components and the risk of IHD. Thus, while making central obesity an essential requirement may make etiological sense and may be relevant to the identification of the insulin-resistant individual, the evidence that this approach is important for the identification of individuals at risk of IHD is limited at this time.

Several factors could also explain our findings. First, central obesity may not cause IHD directly but rather through the associated risk factors and thus may not have a strong influence on the risk of IHD

Table 3—*Risk of IHD for individuals with the metabolic syndrome according to IDF and AHA criteria*

	n of events (%)	Person-years	Incidence rate (per 1,000 person-years)	HR (95% CI)*	HR (95% CI)†
Including diabetic patients					
IDF criteria					
No MetS	76 (2.1)	34,685	2.1 (1.7–2.7)	1.0	1.0
MetS	59 (7.7)	6,716	8.8 (6.6–11.0)	3.9 (2.8–5.5)	2.1 (1.4–3.1)
AHA criteria					
No MetS	44 (1.4)	31,319	1.4 (0.9–1.8)	1.0	1.0
MetS	91 (8.0)	10,082	9.0 (7.2–10.9)	6.3 (4.4–9.0)	2.7 (1.8–4.0)
Excluding diabetic patients					
IDF criteria					
No MetS	58 (1.7)	32,994	1.8 (1.3–2.2)	1.0	1.0
MetS	38 (6.7)	5,013	7.6 (5.2–10.0)	4.2 (2.8–6.3)	2.3 (1.5–3.6)
AHA criteria					
No MetS	40 (1.3)	30,541	1.3 (0.9–1.7)	1.0	1.0
MetS	56 (6.7)	7466	7.5 (5.5–9.5)	5.6 (3.7–8.4)	2.3 (1.5–3.6)

*Unadjusted HRs. †Adjusted HRs for age, study, ethnic group, sex, LDL cholesterol, smoking (nonsmoker vs. current smoker), and alcohol intake (none/occasional vs. ≥1/month). MetS metabolic syndrome.

in this study until after the other CVD (metabolic syndrome) risk factors associated with central obesity have developed. Second, waist circumference is an imperfect surrogate of abdominal adiposity (19), and using it might lead to misclassification of individuals. Finally, central obesity is important, but the threshold for Asians may need to be further lowered.

The underlying purpose for diagnosis of the metabolic syndrome is to identify individuals who are at increased risk of developing diabetes and CVD and to apply preventive measures (1,2). We found in Asians that both individuals with and without central obesity and other metabolic syndrome components are at similar risk of IHD. The current AHA/NHLBI (2) proposal includes all of these individuals, while a sizable number who do not have central obesity but have the metabolic syndrome are omitted by the IDF (1) criteria and thus identifies a greater proportion of those at increased risk of IHD. However, we cannot comment at this time on the relevance of central obesity as an essential component of the metabolic syndrome in relation to the risk of diabetes due to lack of follow-up data. It may well be that the impact differs from that for IHD. Finally, of note is the high proportion of current smokers in the group of individuals without central obesity but with the metabolic syndrome compared with the other two groups. Although this has been adjusted for in the analysis to determine the risk of IHD for each group, it is still important to remember that the focus on the metabolic syndrome should not lead to negligence of the other CVD risk factors that need to be addressed at the individual level.

Possible limitations of our study should be noted. Measurement error of variables, especially waist circumference, could have occurred, though these are likely to be nondifferential leading to an underestimate of risks. Ascertainment of events was done only by data linkage, though three different population-based registers were used allowing for good coverage and case ascertainment. The study comprises two different cross-sectional surveys, though the participants of both were random samples selected using similar methodology.

In conclusion, this study has shown that the risk of IHD is increased in individuals with the metabolic syndrome with or without central obesity. However, the prevalence of metabolic syndrome is increased by 8.5% if central obesity is "optional" rather than "essential" and thus identifies more individuals at risk of IHD. Apart from metabolic syndrome, other CVD risk factors in individuals should also be considered and appropriately managed.

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