A Comparison Of Components of Two Definitions of the Metabolic Syndrome Related to Cardiovascular Disease and All-Cause Mortality in a Cohort Study in Thailand

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The metabolic syndrome, a clustering of metabolic risk factors, has been reported to be associated with the risk of cardiovascular disease (CVD) (1). Questions have been raised about which components of the metabolic syndrome are more strongly associated with CVD (2), whether other combinations of the components have stronger associations (3), and the role of waist circumference in the definition of metabolic syndrome in Asian populations (4), where obesity is typically less common than in the West. We address these questions using data from the Electricity Generating Authority of Thailand (EGAT) Study.

RESEARCH DESIGN AND METHODS

— Details of the EGAT study have been reported elsewhere (5,6). Briefly, a total of 3,499 employees (2,702 men) aged 35–54 years were surveyed in 1985; blood samples were obtained after a 12-h overnight fast. The current analysis is limited to 2,545 men and 671 women with complete baseline data on metabolic and anthropometric measurements and for whom outcomes were available. No subjects had a history of myocardial infarction (MI) or stroke at entry.

According to the Adult Treatment Panel (ATP) III (7), the metabolic syndrome is present if an individual has three or more of the following: high triglycerides, low HDL cholesterol, high blood pressure, high fasting plasma glucose (FPG) or previously diagnosed type 2 diabetes (high FPG), and central obesity. The International Diabetes Federation (IDF) uses the same criteria as ATP III, except with the addition of central obesity as a requirement. To qualify as having the metabolic syndrome, an individual must have central obesity plus any two of the following: high triglycerides, low HDL cholesterol, hypertension, and diabetes (8). Outcomes analyzed were all-cause mortality and CVD (fatal or nonfatal MI or stroke) during a 17-year period (1985–2002). CVD was adjudicated by a committee, using standard criteria for confirmation (9,10).

McNemar's test was used to compare prevalence of the metabolic syndrome by ATP II and IDF definitions. Cox regression models were used to estimate associations with mortality and CVD. All models were adjusted for age, sex, current smoking status (yes/no), current alcohol consumption (yes/no), physical activity (<3 times per week or ≥3 times per week), and income (<5,000, 5,001–10,000, or ≥10,000 baht per month). Areas under receiver-operating characteristics curves (AUCs) were used to compare the predictive performance of models.

RESULTS

— The prevalence of metabolic syndrome in 1985, according to ATP III and IDF, was 19.3 and 11.7% ($P < 0.001$) in men and 11.8 and 10.3% ($P = 0.03$) in women, respectively. Over 17 years, there were 135 (120 male and 15 female) CVD events (3.0 and 1.4 per 1,000 person-years in men and women, respectively) and 309 (276 male and 33 female) deaths (6.8 and 3.0 per 1,000 person-years in men and women). Subsequent analyses were limited to men because there were too few CVD events in women for reliable analyses.

Both metabolic syndrome definitions were more strongly associated with CVD than with all-cause mortality (Table 1). Compared with IDF, the ATP III criteria showed stronger, but not significantly different ($P \geq 0.14$), associations. Among all possible sets of qualifying criteria, the combination of central obesity, high blood pressure, high FPG, and low HDL cholesterol yielded the greatest hazards ratio (HR) for CVD, followed by all five and then by low HDL cholesterol, high blood pressure, and high FPG. When all individual components were cross-adjusted for each other in the same model, only high blood pressure and high FPG were independently associated with CVD and mortality. An additional analysis, excluding those with diabetes at baseline, found that only high blood pressure was independently associated with each outcome.

Regardless of whether participants had central obesity, HRs comparing those with qualifying sets of metabolic syndrome components to those without were

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Abbreviations: ATP, Adult Treatment Panel; AUC, area under receiver-operating characteristics curve; CVD, cardiovascular disease; EGAT, Electricity Generating Authority of Thailand; FPG, fasting plasma glucose; IDF, International Diabetes Federation; MI, myocardial infarction.

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

Table 1—*HRs adjusted for age, smoking status, alcohol consumption, physical activity, income, and AUCs for different definitions and combinations of components of the metabolic syndrome at baseline in men*

		CVD events		All-cause mortality	
Comparison group vs. absence	*n* (%)	HR (95% CI)	AUC (95% CI)	HR (95% CI)	AUC (95% CI)
Definitions of the metabolic syndrome					
Updated ATP III	490 (19.3)	2.41 (1.67–3.51)	0.710 (0.665–0.755)	1.60 (1.23–2.09)	0.702 (0.669–0.735)
IDF	297 (11.7)	2.14 (1.39–3.28)	0.695 (0.648–0.742)	1.39 (1.01–1.91)	0.696 (0.663–0.729)
Qualifying sets of components					
Central obesity, high TG, and low HDL	158 (7.1)	2.12 (1.21–3.74)	0.712 (0.660–0.764)	1.27 (0.81–1.98)	0.693 (0.656–0.731)
Central obesity, high TG, and high BP	180 (8.1)	2.31 (1.37–3.91)	0.711 (0.658–0.764)	1.58 (1.08–2.32)	0.700 (0.664–0.737)
Central obesity, high TG, and high FPG	83 (3.9)	3.05 (1.56–5.95)	0.712 (0.657–0.766)	2.20 (1.37–3.54)	0.712 (0.674–0.749)
Central obesity, low HDL, and high FPG	47 (2.2)	4.24 (2.08–8.64)	0.722 (0.667–0.778)	1.98 (1.10–3.59)	0.705 (0.667–0.743)
Central obesity, low HDL, and high BP	112 (5.2)	2.45 (1.34–4.48)	0.714 (0.660–0.768)	1.26 (0.76–2.09)	0.691 (0.652–0.729)
Central obesity, high BP, and high FPG	74 (3.5)	4.35 (2.38–7.96)	0.722 (0.668–0.776)	2.19 (1.34–3.58)	0.709 (0.671–0.746)
High TG, low HDL, and high BP	219 (9.6)	2.57 (1.59–4.13)	0.716 (0.665–0.767)	1.66 (1.17–2.36)	0.700 (0.644, 0.736)
High TG, low HDL, and high FPG	97 (4.5)	2.93 (1.55–5.53)	0.716 (0.661–0.771)	1.83 (1.13–2.97)	0.707 (0.669–0.744)
High TG, high BP, and high FPG	112 (5.2)	3.16 (1.77–5.63)	0.715 (0.661–0.769)	2.09 (1.38–3.19)	0.712 (0.675–0.748)
Low HDL, high BP, and high FPG	68 (3.2)	4.60 (2.53–8.36)	0.728 (0.673–0.782)	1.93 (1.14–3.28)	0.703 (0.665–0.741)
Central obesity, high TG, high FPG, and low HDL	39 (1.9)	4.01 (1.82–8.84)	0.717 (0.660–0.773)	1.87 (0.95–3.68)	0.705 (0.667–0.743)
Central obesity, high TG, high BP, and low HDL	94 (4.4)	2.25 (1.15–4.41)	0.710 (0.655–0.766)	1.38 (0.81–2.35)	0.694 (0.656–0.733)
Central obesity, high TG, high BP, and high FPG	54 (2.6)	3.92 (1.94–7.92)	0.716 (0.661–0.771)	2.13 (1.21–3.76)	0.708 (0.670–0.745)
Central obesity, high BP, high FPG, and low HDL	29 (1.4)	5.98 (2.80–12.75)	0.723 (0.667–0.780)	2.01 (0.98–4.13)	0.702 (0.664–0.741)
High TG, high BP, high FPG, and low HDL	50 (2.4)	4.39 (2.19–8.83)	0.718 (0.662–0.774)	2.16 (1.20–3.88)	0.706 (0.667–0.744)
Central obesity, high TG, high BP, high FPG, and low HDL	23 (0.9)	5.61 (2.39–13.14)	0.717 (0.659–0.774)	2.00 (0.88–4.55)	0.703 (0.664–0.742)
Each component adjusted for all others					
High TG	1,089 (42.8)	0.96 (0.65–1.41)		1.01 (0.78–1.30)	
Low HDL	801 (31.5)	1.30 (0.88–1.91)		1.13 (0.87–1.47)	
High BP	950 (37.3)	2.15 (1.47–3.15)	0.726 (0.682–0.770)	1.47 (1.15–1.88)	0.710 (0.677–0.743)
Central obesity	461 (18.1)	1.45 (0.96–2.20)		1.03 (0.76–1.39)	
High FPG	411 (16.2)	1.67 (1.11–2.51)		1.57 (1.19–2.07)	

High TG is defined as triglycerides ≥150 mg/dl; high plasma glucose is defined as glucose ≥100 mg/dl or previous diagnosis of diabetes. Low HDL is defined as HDL cholesterol <40 mg/dl; high blood pressure is defined as blood pressure ≥130/85 mmHg or previous diagnosis of hypertension. BP, blood pressure; TG, triglycerides.

between 1.59 and 5.49. Only for the comparison of those with high triglyceride, high blood pressure, and high FPG versus those without were the HRs all significantly different from unity for both outcomes, with and without central obesity. The HRs and AUCs were higher for those with central obesity than for those without central obesity except for the comparison of high triglycerides, low HDL cholesterol, and high blood pressure but not for mortality.

CONCLUSIONS — In this study, the ATP III definition, using the Asian cutoff for waist circumference, produced a higher prevalence of metabolic syndrome and a stronger association with both CVD and all-cause mortality compared with the IDF definition. High blood pressure and high FPG were shown to be the most crucial components of the metabolic syndrome because only these components had independent effects, whereas with the three strongest associations with CVD, all included these two components; adding other components sometimes weakened the effect. It is likely that the effect of high FPG is due to diabetes at baseline or incidence of diabetes afterward. Whereas our findings support the theory that obesity increases the risk of CVD (4), they do not suggest that central obesity is a necessary component of metabolic syndrome because individuals without central obesity also have excess risk factors for CVD and death in this Asian population. This study found that the metabolic syndrome, as defined by either definition, performed no better than many of the models made up of constituent risk factors in predicting or discriminating CVD or all-cause mortality.

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References

1. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salonen JT: The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 288:2709–2716, 2002
2. Kahn R, Buse J, Ferrannini E, Stern M: The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* 28:2289–2304, 2005
3. Asia Pacific Cohort Studies Collaboration, Patel A, Barzi F, Woodward M, Ni Mhurchu C, Ohkubo T, Lam TH, Welborn T: An evaluation of metabolic risks for coronary death in the Asia Pacific region. *Diabetes Res and Clin Pract*. 74:274–281, 2006
4. Katzmarzyk PT, Janssen I, Ross R, Church TS, Blair SN: The importance of waist circumference in the definition of metabolic syndrome: prospective analyses of mortality in men. *Diabetes Care* 29:404–409, 2006
5. Sritara P, Cheepudomwit S, Chapman N, Woodward M, Kositchaiwat C, Tunlayadechanont S, Lochaya S, Neal B, Tanomsup S, Yipintsoi T: Twelve-year changes in vascular risk factors and their associations with mortality in a cohort of 3,499 Thais: the Electricity Generating Authority of Thailand Study. *Int J Epidemiol* 32:461–468, 2003
6. Aekplakorn W, Bunnag P, Woodward M, Sritara P, Cheepudomwit S, Yamwong S, Yipintsoi T, Rajatanavin R: A risk score for predicting incident diabetes in the Thai population. *Diabetes Care* 29:1872–1877, 2006
7. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC, Spertus JA, Costa F, American Heart Association, National Heart, Lung, and Blood Institute: Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 112:2735–2752, 2005
8. Alberti KG, Zimmet P, Shaw J: The metabolic syndrome: a new worldwide definition. *Lancet* 366:1059–1062, 2005
9. Hatano S: Experience from a multicentre stroke register: a preliminary report. *Bull World Health Organ* 54:541–553, 1976
10. Nomenclature and criteria for diagnosis of ischemic heart disease: report of the Joint International Society and Federation of Cardiology/World Health Organization task force on standardization of clinical nomenclature. *Circulation* 59:607–609, 1979