World Health Organization–Defined Metabolic Syndrome Is a Better Predictor of Coronary Calcium Than the Adult Treatment Panel III Criteria in American Men Aged 40–49 Years

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Detection of coronary artery disease, a major cause of death in the U.S., is important in primary prevention settings. The noninvasive screening method of electron beam–computed tomography (EBCT) can be used to quantify coronary arterial calcification (CAC) and identify subjects with subclinical coronary artery atherosclerosis (1,2). However, EBCT screenings of all asymptomatic subjects is not practical in the clinical setting (3,4). Therefore, identification of high-risk subjects before EBCT evaluation is necessary. Currently, the metabolic syndrome, a constellation of risk factors, is used to identify high-risk individuals over and above conventional coronary risk factors because of the independent association of the metabolic syndrome with subsequent development of cardiovascular diseases and diabetes (5–10). The purpose of this study was *1*) to determine whether risk identification using metabolic syndrome as a criterion is useful for the detection of CAC with EBCT and *2*) to compare the usefulness of the National Cholesterol Education Program Adult Treatment Panel III (ATP-III) guidelines (5) definition of metabolic syndrome with the World Health Organization (WHO) (8) definition.

RESEARCH DESIGN AND METHODS

We examined 100 male residents in Allegheny County, Pennsylvania, aged 40–49 years, without evidence of clinical cardiovascular disease, diabetes, cancer, renal failure, or familial hyperlipidemias. The recruitment of the subjects has been described in detail (11). Among the 100 participants, 99 were Caucasian. Informed consent was obtained from all participants, and the study was approved by the University of Pittsburgh's institutional review board.

Measurements included BMI, waist girth, and blood pressure (BP). Blood was collected after a 12-h fast; serum samples were evaluated in the Heinz Laboratory, Department of Epidemiology, University of Pittsburgh. Serum lipids were measured with the standardized methods of the Centers for Disease Control and Prevention, including total cholesterol, HDL choloesterol, and triglycerides. LDL cholesterol was estimated by the Friedewald equation (12). When triglycerides were >400 mg/dl, LDL cholesterol was measured directly using an automated spectrophotometric assay. Fasting serum glucose was determined using the hexokinase-glucose 6 phosphate dehydrogenese enzymatic assay, and insulin was determined using radioimmunoassay (Linco Research, St. Charles, MO). Current medications, smoking status, and demographic data were also collected.

The metabolic syndrome was defined using the ATP-III guidelines (5) and WHO (8) criteria separately. The metabolic syndrome defined by ATP-III guidelines consists of three or more of the following: fasting plasma glucose ≥110 mg/dl, serum triglycerides ≥150 mg/dl, serum HDL cholesterol <40 mg/dl, BP ≥130/85 mmHg or on BP medication, or waist girth >102 cm. We used the modified definition of the WHO criteria (13), consisting of hyperinsulinemia (the upper fourth of the fasting insulin level among nondiabetic subjects) or hyperglycemia (fasting glucose ≥110 mg/dl) in addition to at least two of the following: waist girth ≥94 cm, dyslipidemia (triglycerides ≥150 mg/dl or HDL cholesterol <40 mg/dl), or BP ≥140/90 mmHg or taking BP medication. Coronary calcium scores (CCS) were determined by EBCT using a General Electric Imatron C150 scanner (General Electric Medical Systems, South San Francisco, CA). AccuImage software (AccuImage Diagnostic, San Francisco, CA) and the Agatston scoring method (14) were used to read computed tomography scans.

Logistic regression analysis was used to assess the association between conventional risk factors, metabolic syndrome, and a CCS of ≥10. Significance was defined as $P < 0.05$. We conducted the Hosmer and Lemeshow goodness-of-fit test to assess whether the models significantly predicted CCS of ≥10. For this test, $P >$

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Abbreviations: ATP-III, Adult Treatment Panel III; BP, blood pressure; CAC, coronary arterial calcification; CCS, coronary calcium scores; EBCT , electron beam–computed tomography; WHO, World Health Organization.

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

Table 1—*The relationship between coronary risk factors and coronary calcium by multiple logistic regression models (n = 100)*

Independent variables	Model 1* Estimated odds ratio (95% CI)	*P*	Model 2†‡ Estimated odds ratio (95% CI)	*P*	Model 3‡§ Estimated odds ratio (95% CI)	*P*
Age	1.13 (0.95–1.33)	0.17	1.15 (0.94–1.32)	0.21	1.12 (0.94–1.33)	0.19
Systolic blood pressure	1.05 (1.00–1.11)	0.05	1.05 (1.00–1.10)	0.82	1.06 (1.01–1.12)	0.02
HDL cholesterol	0.99 (0.95–1.33)	0.72	1.01 (0.95–1.03)	0.67	1.01 (0.96–1.05)	0.77
LDL cholesterol	1.00 (0.98–1.02)	0.96	1.00 (0.99–1.02)	0.91	1.00 (0.98–1.02)	0.91
Cigarette smoking	2.89 (0.88–9.57)	0.08	2.90 (0.86–9.78)	0.09	2.95 (0.85–10.2)	0.09
Metabolic syndrome (defined by ATP-III guidelines)	—	—	3.02 (0.72–12.6)	0.13	—	—
Metabolic syndrome (defined by WHO criteria)	—	—	—	—	4.17 (1.15–15.2)	0.03

Dependent variable is CCS ≥10. *Model 1: conventional risk factors are used as independent variables. †Model 2: conventional risk factors and metabolic syndrome (defined by ATP-III guidelines) are used as independent variables. ‡Hosmer and Lemeshow goodness-of-fit test showed that the model predicted the dependent variable. §Model 3: conventional risk factors and metabolic syndrome (defined by WHO criteria) are used as independent variables.

0.05 indicates that the model predicts CCS of ≥10. All statistical analyses were performed using SAS version 8.02 (SAS Institute, Cary, NC).

RESULTS — Univariate logistic regression analysis indicated that only BP was associated with CCS of ≥10. The multiple logistic regression model containing only conventional risk factors did not predict CCS of ≥10 ($P = 0.03$). The models that included either of the two definitions of metabolic syndrome along with conventional risk factors significantly predicted CCS of ≥10 ($P = 0.58$, and $P = 0.49$). No significant association was found between CCS of ≥10 and each of the independent variables in the model with metabolic syndrome, as defined by ATP-III guidelines, in addition to conventional risk factors. However, systolic BP and WHO-defined metabolic syndrome were both found to be significantly associated with CCS of ≥10 in the model with metabolic syndrome defined by WHO criteria (Table 1).

CONCLUSIONS — We found a significant association between CCS of ≥10 and metabolic syndrome as defined by WHO criteria but not metabolic syndrome as defined by ATP-III guidelines. Previous studies showed the significant relationship between subclinical atherosclerosis and metabolic syndrome by both the WHO and ATP-III (15–17) guidelines. Insulin resistance was regarded as a mechanism of this relationship (16). Lack of a criterion for hyperinsulinemia in the ATP-III guidelines definition may be an explanation for our inability to detect the association between CCS of ≥10 and metabolic syndrome as defined by ATP-III guidelines. A recent study using the glucose clamp technique reported that metabolic syndrome defined by ATP-III guidelines did not identify insulin resistant individuals (18). Hyperinsulinemia, which is often involved in insulin resistance, may accelerate atherosclerosis (19,20). Therefore, metabolic syndrome defined by WHO criteria may be a more powerful definition for detecting CAC than metabolic syndrome defined by ATP-III guidelines.

Small sample size, voluntary subject selection bias, narrow subject age range, and the nature of a cross-sectional study were limitations of this study. However, we would expect the risk relationship to be similar to that in a random population because the participants of this study are unlikely to have previous knowledge of their CCS. Also, the subject age typically precedes the onset of coronary artery disease (21).

In conclusion, the concept of metabolic syndrome, especially the WHO definition, may be helpful in predicting CAC in healthy young men over and above conventional risk factors. A larger sample size and longitudinal study design are required for definitive evaluation.

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