Risk Associated With the Metabolic Syndrome Versus the Sum of Its Individual Components

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Current guidelines for the prevention of cardiovascular disease (CVD) encourage identification of the metabolic syndrome (a clustering of CVD risk factors) in clinical practice (1,2), but an important unanswered question is whether the metabolic syndrome predicts risk above and beyond its individual components (3). We investigated this issue using a large cohort of men examined on two occasions 20 years apart and followed for a maximum of 32.7 years.

RESEARCH DESIGN AND METHODS

— In a community-based cohort of men of the same age (available at www.pubcare.uu.se/ULSAM) (4), we investigated four baseline samples: two defined at age 50 years (the whole cohort [n = 2,322] and a primary preventive sample [n = 2,198], excluding people with a myocardial infarction, stroke, or diabetes at or before baseline) and two at a reexamination at age 70 years (the whole cohort [n = 1,221] and the primary preventive sample [n = 872]), as the impact of the metabolic syndrome may vary with age and risk level (4). Informed consent was obtained, and the Uppsala University Ethics Committee approved the study.

Baseline examinations and National Cholesterol Education Program definitions of the metabolic syndrome have been previously published (4). Analyses using the age-50-years baseline had a maximum of 32.7 years of follow-up (median 29.8 years, 60,347 person-years at risk [PYAR]). Analyses from age 70 years had a maximum of 11.4 years of follow-up (median 9.1 years, 10,455 PYAR). The outcome (cardiovascular death, ICD-9 codes 390–459, ICD-10 codes I00–I99) was defined using the Swedish national cause-of-death register.

We tested the hypothesis that the metabolic syndrome predicts cardiovascular mortality better than the sum of its components in two ways: comparing areas under receiver-operating characteristics curves (C-statistics) and using likelihood ratio tests. Logistic regression models containing the individual metabolic syndrome components were fitted to the total and primary preventive samples for each baseline. Thereafter, the metabolic syndrome variable was added. C-statistics were calculated for all models, and we then compared the C-statistics of models with and without the metabolic syndrome variable. Similarly, Cox proportional hazards models were fitted to the total and primary preventive samples for each baseline. Likelihood ratio tests were used comparing Cox models including only the individual metabolic syndrome components to models also including the metabolic syndrome variable. All analyses were defined a priori. Stata 8.2 (StataCorp, College Station, TX) was used for all analyses.

RESULTS

— The metabolic syndrome was present in 17.8% of the cohort (15.9% of the primary preventive sample) at age 50 years and in 23.2% of the cohort (15.8% of the primary preventive sample) at age 70 years. In the total sample, 502 participants died from CVD (rate 8.3/1,000 PYAR) after the examination at age 50 years and 133 (rate 12.7/1,000 PYAR) after age 70 years.

The metabolic syndrome did not predict cardiovascular mortality independently of its individual components at any age and in any sample in the present study, irrespective of the method used (likelihood ratio test or comparing C-statistics) (Table 1).

CONCLUSIONS

— In this community-based cohort of men with long follow-up, the metabolic syndrome did not provide risk information above and beyond its individual components. In a previous study in the elderly (5), the metabolic syndrome apparently predicted a composite CVD end point independently of its components, although this question was not formally investigated. The metabolic syndrome predicts mortality independently of established CVD risk factors (4) and may thus merit attention in the clinical setting, but if the results of the present study are confirmed in other samples, the metabolic syndrome might be viewed as a clinically handy summary measure of nontraditional risk factors rather than as a strong biological entity.

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Abbreviations: CVD, cardiovascular disease; PYAR, person-years at risk.

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

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Table 1—*Predictive value of the metabolic syndrome versus its components at ages 50 and 70 years for cardiovascular mortality*

	Age 50 years		Age 70 years	
	Total sample	Primary preventive sample	Total sample	Primary preventive sample
Cox models				
Metabolic syndrome (versus not), unadjusted	2.20 (1.81–2.67)	2.04 (1.65–2.52)	1.92 (1.34–2.73)	1.28 (0.71–2.29)
Metabolic syndrome components, adjusted for each other				
High glucose (versus not)	1.16 (0.94–1.44)	1.02 (0.79–1.31)	1.71 (1.16–2.50)	1.46 (0.67–3.20)
High blood pressure (versus not)	1.92 (1.55–2.38)	1.88 (1.51–2.34)	1.42 (0.76–2.65)	2.01 (0.80–5.00)
High triglycerides (versus not)	1.28 (1.06–1.54)	1.27 (1.05–1.54)	1.43 (0.98–2.10)	1.14 (0.65–2.00)
Low HDL cholesterol (versus not)	1.51 (1.22–1.89)	1.42 (1.12–1.79)	1.08 (0.73–1.61)	0.98 (0.55–1.74)
Obesity (versus not)	1.65 (1.27–2.15)	1.57 (1.17–2.10)	1.53 (1.03–2.27)	1.60 (0.90–2.83)
Metabolic syndrome (versus not), adjusted for its components	1.14 (0.81–1.61); LR test $P = 0.46$*	1.26 (0.87–1.82); LR test $P = 0.23$*	0.74 (0.37–1.49); LR test $P = 0.40$*	0.52 (0.18–1.48); LR test $P = 0.22$*
Logistic regression models				
Models including only the individual metabolic syndrome components	C 0.62 (0.59–0.65)	C 0.61 (0.58–0.64)	C 0.61 (0.54–0.67)	C 0.56 (0.51–0.62)
Models including individual components plus metabolic syndrome variable	C 0.62 (0.59–0.65); $P = 0.79$†	C 0.61 (0.58–0.64); $P = 0.94$†	C 0.62 (0.58–0.66); $P = 0.66$†	C 0.59 (0.50–0.67); $P = 0.58$†

Data are Cox proportional hazard ratios (95% CI) and C-statistic (area under the receiver-operating characteristic curve). *Likelihood ratio (LR) test *P* values comparing models including only the individual metabolic syndrome components to models also including the metabolic syndrome variable. †*P* values for comparisons of C-statistics for models including only the individual metabolic syndrome components to models also including the metabolic syndrome variable.

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