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Presence of the Metabolic Syndrome Is Not a Better Predictor of Cardiovascular Disease than the Sum of its Components: Data from the D:A:D Study

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Background: The metabolic syndrome is a cluster of cardiovascular disease (CVD) risk factors thought to be associated with a 2-fold increased risk of CVD in the general population. It is much debated whether the metabolic syndrome (defined as ≥ 3 risk factors) contributes additional information over and above that provided by the individual risk factors alone. In a population of HIV infected persons, we investigated whether combinations of risk factors lead to a higher than expected CVD risk.

Methods: Prospective multi-national cohort study of 23,236 HIV-infected subjects. The effect of combinations of components of the metabolic syndrome for the risk of a composite CVD endpoint (myocardial infarction, stroke, and invasive procedures) was assessed by Poisson regression by incorporating interactions between each pair of risk factors (adjusting for age, sex, family history of CVD, smoking status, calendar year, and exposure to cART). We considered triglycerides ≥ 1.7 mmol/L, HDL cholesterol ≤ 1.0 mmol/L in men, ≤ 1.3 mmol/L in women (HDL), systolic blood pressure >130 or diastolic blood pressure >85 mmHg, body mass index >25 kg/m², and a diagnosis of diabetes mellitus. The results were validated in a dataset of $n = 10,143$ individuals.

Results: An increased CVD risk was found with increasing number of concomitant risk factors (unadjusted relative rate per additional factor: 1.70, 95%CI 1.50 to 1.93). When exploring pairwise combinations, the highest CVD rates (per 100 persons years) were seen in patients with high blood pressure and body mass index (3.27 vs 0.46 in patients with no high blood pressure and normal body mass index, diabetes mellitus, and decreased HDL (3.26 vs 0.54 in patients with no diabetes mellitus and normal HDL), high blood pressure and elevated triglycerides (3.01 vs 0.34 in patients without high blood pressure and with normal triglycerides) and diabetes mellitus and elevated triglycerides (2.47 vs 0.37 in patients with normal triglycerides and no diabetes mellitus). There were no positive interactions between the pairwise combinations of risk factors. After adjusting for each of the individual risk factors as well as other confounders, there was no independent association with having metabolic syndrome (1.03, 95%CI 0.63 to 1.68).

Conclusions: There is a strong correlation between the number of the components of the metabolic syndrome observed together in individual patients and CVD risk. However, when seen together, the combined effect of these factors for the risk of CVD is comparable to that expected by multiplying their individual effects. Thus, presence of metabolic syndrome in HIV appears not to increase the CVD risk over and above that conferred by the components of the syndrome separately.