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Inflammation and the Metabolic Syndrome: Clustering and Impact on Survival in a Swedish Community-Based Cohort of 75 Year Olds

Topic 2 – Learning more from what we already know

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Introduction

Cardiovascular disease is a major cause of morbidity and mortality in the developed world. As risk factors have been identified, more than one risk factor has been observed in many individuals. Such clustering of risk factors has been extensively studied| special interest has been focused on the clustering of risk factors in the Metabolic Syndrome (MetS). According to most commonly used definitions this syndrome is defined by cut-off points in: fasting glucose, triglycerides, high density lipoprotein (HDL) cholesterol, waist, and systolic/diastolic blood pressure. High blood concentrations of inflammatory markers, including white blood cell (WBC) count, are closely related to the MetS. Both conditions predict dismal survival. We determined prospective associations between mortality and factors derived by a factor analysis of WBC count and the components of MetS.

Methods / Problem statement

We performed a factor analysis of WBC count and the continuous components of MetS in 196 men and 200 women comprising 65% of all 75-year-olds from the Swedish city Väster&aring|s. Principle component analysis was used to identify an initial set of uncorrelated factors. Skewed variables were log-transformed and variables known to be negatively associated with mortality were inverted prior to the analysis. Varimax rotation, which results in factors with high factor loadings for a few variables and near zero loadings for the remaining, was applied to get more easily interpretable solutions. Cut-off for factor loadings was set at 0.3. Nonparametric bootstrap was used to assess the consistency and accuracy of the factor analysis and calculate confidence intervals. Prospective associations of the factors with all-cause mortality (median follow-up 10.6 years) were assessed by Cox proportional hazard regression. A best subset approach, using the Bayesian information criterion (BIC) as performance measure, was used to identify an optimal set of significant confounders. The predictive ability of the original components and the derived factors was assessed by the time dependent area under the receiver operating characteristic (AUROC) curve.

Results / Proposed solution

The analysis consistently revealed three factors in men and two in women, explaining in median 66% of the total variation in men and 57% in women. Factor 1 included fasting glucose, HDL-cholesterol, triglycerides and waist in men and in addition WBC count in women. Factor 2 included diastolic and systolic blood-pressure in both sexes. In men factor 3 included fasting glucose and WBC count. During follow-up 91 (46%) men and 58 (29%) women died. Factor 1 was significantly related to 10-year mortality in men| hazard ratio (HR) = 1.22 / SD-unit (95%CI: 1.06-1.41, p=0.007) and in women| HR = 1.25/SD-unit (95%CI: 1.06-1.48, p = 0.010). In a pooled analysis the HR for factor 1 was 1.16 / SD-unit (95%CI: 1.04-1.29, p = 0.010) adjusting for sex, previous myocardial infarction, known hypertension and current smoking, the only significant confounders using BIC. The time dependent AUROC curve after 10 year increased from 0.58 to 0.70 adding factor 1 to the confounders. In men factor 3 was significantly related to 10-year mortality| HR=1.29 / SD-

unit (95%CI: 1.07-1.56, p = 0.009) and almost significant after adjusting for previous myocardial infarction, known hypertension and current smoking| HR = 1.20 / SD-unit (95%CI: 1.00-1.44, p = 0.055).

Conclusions

By including WBC count in a factor analysis of the MetS components, metabolic-inflammatory factor/factors closely related to survival were revealed. This finding adds to previous clinical evidence of a close relationship between the metabolic syndrome and low-grade inflammatory activity.