P3642

Predictive value of soluble urokinase-type plasminogen activator receptor for cardiovascular death and non-fatal myocardial infarction in patients with coronary artery disease

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Introduction: Stratification for subsequent coronary events among patients with coronary artery disease (CAD) is of considerable interest due to the potential to guide secondary preventive therapies. Soluble urokinase-type plasminogen activator receptor (suPAR) is expressed on various cells involved in atherogenesis and plaque instability, and has been associated with poor clinical outcomes in patients with various conditions.

Purpose: In this study we investigated the potential role of suPAR as a prognostic biomarker for adverse outcome in patients with CAD, and acute coronary syndrome (ACS) in particular.

Methods: Plasma levels of suPAR were measured in a cohort of 1,703 patients (AtheroGene Study) with documented coronary artery disease – including 626 patients with ACS and 1077 patients with stable angina pectoris (SAP). The main outcome measures were defined as cardiovascular death and non-fatal myocardial infarction (MI). Survival curves for the endpoints considered were computed according to thirds of the suPAR distribution. The equality of survival curves was tested using the log-rank test. Multivariable models adjusted for common cardiovascular risk factors and the biomarkers CRP, NT-proBNP and high-sensitivity troponin I (hs-TnI) in particular were also computed.

Results: The prognostic utility of suPAR was evidenced by survival curves stratified for tertiles of circulating suPAR levels –both, in the overall cohort ($p=0.00062$), and in the ACS cohort ($p=0.00099$) with a median follow-up of 3,5 years. In multivariable-adjusted Cox regression analyses the hazard ratio (HR) for the prediction of cardiovascular death was 3.60 for log-transformed suPAR levels ($p<0.001$) in the overall CAD cohort, whereas it was 3.34 ($p=0.003$) in the ACS cohort. The HR regarding prediction of the combined outcome cardiovascular death and/or non-fatal MI during follow-up was 2.19 ($p<0.001$) in the overall cohort, and 2.56 ($p<0.001$) in the ACS cohort. After multivariate adjustment, including conventional cardiovascular risk factors and hs-TnI, suPAR, after log transformation, still enabled a reliable and strong prediction of future cardiovascular death with a HR of 3.17 ($p<0.001$) in the overall CAD cohort, and a HR of 2.85 ($p=0.014$) in the ACS cohort.

Conclusions: Our study demonstrates that suPAR has a strong prognostic value independent of hs-TnI in secondary prevention settings, and thereby might represent a valuable biomarker for risk estimation in CAD.