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Institutionen för molekylär medicin och kirurgi

Inflammatory markers and prognosis in Acute Coronary Syndromes

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Abstract

Background: Inflammation both accelerates atherosclerosis and contributes to the activation and rupture of the atherosclerotic plaque. Several markers of inflammation, such as CRP, have shown prognostic merit in patients with acute coronary syndromes (ACS).

Aims: To investigate the association between circulating levels of some markers with relation to inflammation – osteoprotegerin (OPG), Chemokine (C-X-C motif) ligand 16 (CXCL16) and chromogranin A (CgA) – and prognosis in a population of patients with ACS.

Material and methods: Patients aged 18-79 years who were admitted to the coronary care unit at a university hospital with an ACS had blood drawn within 24 hours and after 3 months; echocardiography with determination of the left ventricular ejection fraction (LVEF) was performed within 5 days of admission. Mortality data were obtained from the Swedish National Population Registry and morbidity data from the Swedish Hospital Discharge Registry. The length of follow-up was a median of 81-92 months.

Results: Higher OPG levels were associated with an increased likelihood of ST-elevation myocardial infarction (MI), markers of myocardial damage and indices of cardiac dysfunction such as LVEF and B-type natriuretic peptide (BNP). The patients with the higher levels were also more likely to have a history of heart failure (HF) and to be hypotensive on arrival. The circulating OPG levels were predictive of long-term mortality and the incidence of rehospitalization due to HF, a relationship that remained significant after adjustment for clinical risk factors and, in a subgroup where such data were available, after further adjustment for LVEF, CRP, BNP and troponin. The C-statistics of the prognostic information offered by OPG were significantly better than CRP and troponin and similar to BNP and LVEF. For CXCL16, as for OPG, higher levels were associated with higher age and STEMI. CXCL16 predicted long-term mortality, future hospitalizations for HF and new MI, also after adjustment for clinical risk factors. After further adjustments for LVEF, CRP, proBNP and troponin, only the combination of OPG and CXCL16 serum levels predicted cardiovascular (CV) and all-cause mortality, as well as HF rehospitalizations. This was true for both the long term and short term, even after adjustment for the Global Registry of Acute Coronary Events (GRACE) score. Serum levels of OPG and CXCL16 at day 1 and 3 months after ACS were similarly associated with outcome.

CgA was also an independent predictor of mortality and HF after adjustments for conventional risk factors, including troponin, and was still significantly associated with mortality after further adjustment for LVEF and proBNP.

Conclusions: Even after adjustment for conventional risk markers, serum levels of OPG, CXCL16 and CgA were predictive of long-term mortality and rehospitalizations due to HF in patients with ACS. We also found that a combination of OPG and CXCL16 serum levels was predictive of mortality and HF hospitalizations - and gave more information than each marker alone - in both the long term and the short term, even after adjustment for the GRACE score. Inflammatory markers appear to add prognostic value above and beyond clinical information.

Key words: acute coronary syndrome, prognosis, atherosclerosis