Cardiovascular and inflammatory biomarkers for non-invasive detection of coronary artery obstruction and prediction of long-term survival in patients with suspected chronic coronary syndrome


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Introduction and methods: The knowledge about diagnostic and prognostic value of cardiac and inflammatory biomarkers in patients with chronic coronary syndrome (CCS) is limited. To address this, we analyzed serum levels of selected biomarkers in 2536 patients with suspected CCS (35% female) from the Leipzig LIFE Heart Study who were admitted for coronary angiography. The median follow-up was 10 years. The following biomarkers were considered: high sensitive troponin T (hsTNT), N-terminal pro B-type natriuretic peptide (NT-proBNP), copeptin, high sensitive C-reactive protein (hsCRP) and interleukin-6 (IL-6). Patients were stratified according to the angiographic severity of coronary artery disease (CAD): CAD0 (no sclerosis), CAD1 (non-obstructive, i.e., stenosis < 50%), CAD2 (≥ one stenosis ≥ 50%). Group comparison (GC) included GC1: CAD0 + 1 vs. CAD2, GC2: CAD0 vs. CAD1 + 2. Using age-, sex and symptom-based pre-test probability (PTP) table for obstructive CAD (i.e. CAD 2) which was published in the current CCS guidelines, patients were further classified into the following three categories: PTP < 5% (n=559), PTP 5-15% (n=545) and PTP > 15% (n=1432).

Results: CAD0, CAD1, CAD2 were apparent in 999, 529, and 1008 patients, respectively. Upon adjustment for traditional risk factors (TRF) the levels of hsTNT, NT-proBNP and IL-6 showed significant difference in GC1 (hsTNT: p=2.0x10-10, NT-proBNP: p=0.049, IL6: p=0.030). In GC2 only elevated hsTNT remained significant (p=1.9x10-7). In the ROC analysis only hsTNT slightly improved the AUC for the GC1-comparison in addition to TRF (0.729 with vs 0.712 with hsTNT, p=0.013). Within the PTP subcategories the following results were obtained: PTP < 5%: AUC 0.747 with vs 0.730 without hsTNT, p=0.017; PTP 5-15 %: AUC 0.636 with vs 0.670 without hsTNT, p<0.001; PTP > 15%: AUC 0.699 with vs 0.677 without hsTNT, p=0.024). In PTP 5-15% subgroup TropT cut-off value < 3 pg/mL (N= 119 / 23.4%) showed sensitivity of 89.7% and specificity of 73.1% for CAD2 detection.

Ten years survival in groups CAD0, CAD1, CAD2 were 88.3%, 77.3%, 72.4%, respectively. In the multivariate analysis elevated hsTNT, NT-proBNP, copeptin and IL-6 remained significant mortality predictors in CAD2 patients with hazard ratios of similar magnitude (i.e. 1.5, 1.3, 1.4 and 1.3 per unit on the log-scale of the parameters, respectively). hsCRP did not reach significance. In the model stratified into tertiles according to the effects of classical risk factors and the joint biomarker levels for except hsCRP, hazard rates were 3.13 (tertile 2 vs 1) and 11.2 (tertile 3 vs 1).

Conclusions: In the present study hsTNT substantially improved the detection of obstructive CAD particularly in patients with intermediate PTP 5-15%. Furthermore, the studied biomarkers enable fast and precise non-invasive prediction of mortality risk in patients with suspected CCS, allowing tailored primary and secondary CAD prevention in this high-risk group.