Interleukin-6 plasma levels are elevated in patients with acute myocardial infarction and predict death or recurrent infarction within 1 year - a case-control study

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Background: Acute myocardial infarction (AMI) harbours marked inflammatory components. While cytokines of the same family have been causally related to patient outcome, the role of interleukin (IL)-6 in AMI remains incompletely understood. Recent trials suggest benefits of inhibiting IL-6 in patients with ST-segment elevation myocardial infarction (STEMI). In patients at high atherosclerotic risk, IL-6 blockade reduces markers of inflammation and thrombosis.

Purpose: This study aimed to assess the levels of IL-6 in AMI patients and their predictive value.

Methods: 160 cases (recurrent AMI or death within 1 year) and 160 matched controls were selected from the prospective, multicentric SPUM-ACS Cohort. All patients had an AMI (STEMI or NSTEMI) as initial event and underwent percutaneous coronary intervention (PCI) within 24h of symptom onset. Blood samples were drawn before PCI and biomarker plasma levels were assessed (mesoscale). Comparisons were made with age- and sex-matched healthy blood donors (HD). IL-6 levels are presented as medians and interquartile ranges. Cases, controls and HD were compared using the Kruskal-Wallis test. Correlations of baseline variables to IL-6 levels within cases and controls were assessed by linear regression analyses. Patients were divided into those with higher or lower IL-6 levels according to the median IL-6 level. Kaplan-Meier (KM) analyses for the combined endpoint of death or recurrent AMI were performed.

Results: The overall median IL-6 level was 21.3pg/ml. Patients with higher IL-6 had more previous AMI (n=22, 14%) than patients with lower IL-6 (n=12, 7%, p=0.045). Patients with increased IL-6 had more previous PCI (n=30, 20%) than patients with lower IL6 (n=19, 11%, p=0.045). Both cases and controls showed higher levels of IL-6 than HD (cases: 25.7pg/ml [14.8–81.6], controls: 20.0pg/ml [11.3–40.1], HD: 5.9pg/ml [3.6–9.9]; cases/controls vs. HD: p<0.0001). Among AMI patients, cases showed higher IL-6 levels than controls (p=0.030) (Figure 1).

Within cases and controls, IL-6 was related to IL-1beta (r=0.628, p<0.001), IL-1alpha (r=0.174, p=0.002) and IL-1 receptor antagonist (r=0.422, p<0.001). IL-6 was related to neutrophil/lymphocyte ratio (r=0.147, p=0.016), but not to high-sensitivity C-reactive protein (r=0.087, p=0.142) or N-terminal pro B-type natriuretic peptide (r=0.091, p=0.118). IL-6 was related to Killip Class upon presentation (r=0.190, p<0.001).

KM analyses showed significantly higher rates of death or recurrent AMI within 1 year for patients with higher IL-6 (log-rank p=0.006, Figure 2), with early divergence of the curves.

Conclusions: IL-6 is markedly higher in patients with AMI compared to healthy controls and predicts death or recurrent AMI within 1 year. IL-6 might be a valuable target for early anti-inflammatory therapy to patients with AMI. A deeper understanding of factors influencing IL-6 levels may help select those patients that will benefit most from such treatment.

Figure 1: Cases vs. Controls vs. HD
Figure 1: Kaplan-Meier Analysis