



Analysis of new biomarkers and their kinetics in connection with ST-elevation myocardial infarction and percutaneous coronary intervention

av

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Abstract

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This thesis studies different biomarkers in a cohort of patients suffering from ST-elevation myocardial infarction (STEMI) who underwent Percutaneous coronary intervention (PCI) in Örebro in 2011-2012. Blood samples were collected at three time points, at the arrival at the hospital, 1-3 days after PCI and for a smaller group of patients also 3 months after PCI. The study is a sub-study of the TASTE study, so half of the patients were also randomized to thrombus aspiration in conjunction with their PCI. For all patients, it was also recorded whether the culprit coronary vessel was totally occluded or partially patent. In total, there are samples from 165 patients, but not all markers have been measured in all patients, and 3-month samples are only available from those who had their follow-up in Örebro. The plasma levels of the biomarkers have also been measured in plasma from blood donors for comparison. In March 2019, a follow-up was made of the patients' survival, and the time of death was noted in cases where this had occurred.

The markers studied are the lysosome protein Cathepsin S (Cat-S), the platelet granule protein thrombospondin 1 (TSP-1), the pentraxins C-reactive protein (CRP) and pentraxin 3 (PTX3), the endopeptidase neprilysin, the soluble forms of TNF-receptor 1 and 2 (sTNFR1 and sTNFR2), markers showing activation of the lectin pathway for complement activation (MASP-1/AT, MASP-1/C1-INH, MASP-2/C1-INH, MASP-2/AT) and common activation markers for complement activation (C3a and sC5b-9).

In summary, the thesis shows that the plasma levels of all markers, except neprilysin and sC5b-9, are elevated at the time of arrival compared to healthy blood donors. Neprilysin is at the same level, and sC5b-9 is lower compared to blood donors. 1-3 days after PCI, the levels for CRP, sTNFR1 and sC5b-9 have risen strongly (>50%) compared to the levels at arrival. MASP-1/AT and MASP-2/AT have fallen moderately (about 50%), Cat-S and TSP-1 have decreased strongly, while the remaining markers are relatively similar to the levels at arrival (\pm 25%). The levels for CRP, PTX3, sTNFR1, sTNFR2 and neprilysin decreased even further between 1-3 days and 3 months, sC5b-9 rises slightly while the other markers remain at roughly the same levels. At 3 months, most markers still show higher levels compared to corresponding levels in blood donors, only MASP-2/C1-INH has the same level, while neprilysin is slightly lower and TSP-1 much lower compared to blood donors (the latter presumably an effect of ongoing medication with platelet inhibitors in the patients). No relevant differences were observed between patients with and without thrombus aspiration, and few differences were seen between patients with occluded or partially patent vessels. This may indicate that these factors were of minor importance for the levels of the analyzed markers. In contrast, analysis of survival showed that individuals with plasma levels above the median value for PTX3, sTNFR1 and sTNFR2 at admission and/or at 1-3 days had a significantly increased mortality compared to those with levels below the median value, which indicates that these markers could be interesting for further studies in a material where also analysis of possible interfering factors can be implemented.

Keywords: STEMI, PTX3, sTNFR1, sTNFR2, Cathepsin S, MASP-1/AT MASP-1/C1-INH, MASP-2/AT, MASP-2/C1-INH

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