CAD patients with renal insufficiency: insights into their platelet prothrombotic, transcriptomic and proteomic profile

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Patients with renal insufficiency (RI) present an higher risk to develop coronary artery disease (CAD) (1-3); renal insufficiency is the most important independent predictor of adverse prognosis of cardiovascular events (4).

RI causes modifications in platelet reactivity leading to an higher rate of thrombotic complications compared to CAD patients without this pathology. Few years ago, our group showed that platelet-associated Tissue Factor (pTF) is increased in non-ST elevation acute coronary syndrome (NSTE-ACS) patients (5) and platelet transcriptome is also modified compared to healthy subjects (6).

In this study, we compared pTF expression, platelet-specific gene expression pattern and plasma proteome profile in NSTE-ACS and stable angina (SA) patients with or without RI.

We have enrolled 58 NSTE-ACS patients with RI and 164 without RI, and 34 SA patients with RI and 161 without RI.

pTF was evaluated by whole blood flow cytometry, platelet transcriptome by Illumina Human BeadChips and plasma protein changes by 2-dimensional electrophoresis (2-DE).

The percentage of TF-positive platelets was significantly lower in NSTE-ACS patients with RI compared to subjects without RI (3.65 ± 1.17 and 4.69 ± 0.8, respectively). A similar trend, although not reaching the statistical significance, was present also in SA patients with RI compared to patients without RI.

Differential expression analysis of the platelet transcriptome showed that 28 genes were at least 1.5-fold increased and 16 genes decreased in NSTE-ACS patients with RI ($p<0.01$). The expression levels of 87 genes correlated with the severity of RI: 68 genes positively and 19 genes negatively ($p<0.01$).

Comparison of the 2-DE maps revealed significant differences among the two groups in the expression of 10 plasma proteins; in particular, in NSTE-ACS patients with RI, there was the down-regulation of Fetuin-A, a plasma protein important for the regulation of Calcium.

So, the lower amount of TF-positive platelet found in NSTE-ACS patients with RI may indicate an ongoing activation. Two molecular pathways appeared to be affected by RI: extracellular matrix-receptor interaction may be up-regulated, while translational elongation genes were down-regulated. Finally, plasma proteins, identified by proteomics, may have relevance as candidate biomarkers of clinical prognosis.

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