Neutrophil activation and neutrophil extracellular traps in STEMI patients treated with therapeutic hypothermia

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Topic(s):
Thrombosis, Bleeding

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S140

Introduction
Myocardial infarction (MI) is one of the leading causes of death and morbidity worldwide. Therapeutic hypothermia is successfully used in patients with cardiac arrest. Cardioprotective mechanisms of therapeutic hypothermia in MI are under discussion. In previous work, we described the importance of neutrophils, neutrophil extracellular traps (NETs) and deoxyribonuclease activity in the pathomechanism of MI.

Purpose
In the present project, we evaluated neutrophils and NET markers in the STATIM (Strategic TArget Temperature management In Myocardial Infarction) trial in ST elevation MI (STEMI) patients treated with therapeutic hypothermia and normothermic controls.

Methods
The STATIM trial investigated the impact of therapeutic hypothermia during STEMI, aiming at a temperature below 35°C during reperfusion. 120 patients underwent a 1:1 randomization and blood samples were obtained from first medical contact to 72h after percutaneous coronary intervention (PCI). Additionally, samples from the culprit lesion site (CLS) during PCI were taken. Samples were processed for cell culture, ELISA and flow cytometry analysis.

Results
Neutrophil count, neutrophil activation markers and ex vivo neutrophil migration were not different between patients with and without therapeutic hypothermia. All patients displayed significantly increased numbers of neutrophils at the CLS. Double stranded DNA (dsDNA), a surrogate marker for NET burden, was significantly increased at the CLS in both groups. Levels of dsDNA increased significantly from first medical contact to 72h in patients treated with therapeutic hypothermia, but not in normothermic patients (Figure 1). CLS neutrophil levels correlated positively with CLS dsDNA levels in patients with hypothermia but not in normothermic patients. CLS and 72h post PCI dsDNA levels correlated significantly with CKMB area under the curve, an enzymatic measure of infarct size. Neutrophil count at the time of PCI and 72h post PCI correlated significantly with respective nucleosome levels in the therapeutic hypothermia but not in the control group.

Conclusion
Present data indicate increased NET release in patients treated with therapeutic hypothermia. The addition of specific NET surrogate marker and deoxyribonuclease activity measurements will complement present data. Correlation with cardiac magnet resonance data of infarct size will help to identify clinical significance of present findings.

Figure 1: Double-stranded DNA (dsDNA) levels in STEMI patients in the STATIM trial. Significant increase of dsDNA levels from first medical contact (FMC) until emergency admission and 72h after percutaneous coronary intervention (PCI).
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Figure 1: Double-stranded DNA (dsDNA) levels in STEMI patients in the STATIM trial. Significant increase of dsDNA levels from first medical contact (FMC) until emergency admission and 72h after percutaneous coronary intervention (PCI), (n=47 vs. 46, ****p<0.0001).