

Correlations between systemic inflammation, altered parietal kinetics and ventricular remodeling after acute myocardial infarction

Scientific coordinator: Prof. Univ. Dr. Theodora Benedek

PhD Student: Fărcas-Hîngan (Morariu) Mirabela-Bianca

Acute myocardial infarction (IMA), the most common form of coronary atherosclerotic disease, with a devastating potential in terms of mortality, morbidity and socioeconomic implications. Sequential inflammatory response to IMA plays a critical role in determining the extent of the infarct area, respectively, in the subsequent adverse ventricular remodeling process, constituting a potential target of therapeutic strategies to improve the post-infarction clinical response.

The present PhD thesis proposes to evaluate the impact of an augmented inflammatory status in the post-infarction period, quantified by determining the serum levels of hs-CRP, on the degree of myocardial scar enlargement at 1 month after the acute coronary event, assessed through cardiac MRI imaging among patients who benefited from percutaneous coronary revascularization.

Another objective of the present paper is to evaluate the impact of inflammatory response from acute phase of post-infarction period, determined on the basis of plasma levels of hs-CRP, on structural and functional remodeling processes of the left ventricle, evaluated on the basis of speckle tracking echocardiography and cardiac MRI.

This research is a prospective, non-randomized, observer study that tracked 100 patients with STEMI acute myocardial infarction who benefited from percutaneous emergency coronary revascularization at the culprit lesion and were divided into two sub-studies as follows: - sub-study 1 - which included 75 patients with STEMI acute myocardial infarction and sub-study 2, which included 25 patients presenting in the therapeutic window of STEMI.

Sub-study 1 tracked the correlations between acute inflammatory response and the extent of myocardial infarction in patients with primary coronary revascularization.

The study population was divided into 2 groups according to the baseline plasma level of hs-CRP as follows: Group 1 - 37 patients with a low level of hs-CRP, respectively Group 2 - 38 patients presenting a level

high level of hs-CRP. Subsequently, the study population was divided on the 5th day of hsCRP in Group A - 35 patients with a low level of hsCRP, respectively Group B - 40 patients with a high level of hsCRP.

The group of patients with a high level of baseline hs-CRP showed a greater extension of the infarct area quantified 1 month after the acute event, based on MRI examination. This difference consisted both volumetrically (Group 1 - $20.02 \pm 11.50\text{mL}$ vs. Group 2 - $36.31 \pm 21.03\text{mL}$, $p = 0.0003$), mass (Group 1 - $21.12 \pm 13.59\text{g}$ vs. Group 2 - $37.33 \pm 25.02\text{g}$, $p = 0.0003$), or the percentage of infarct area extension (Group 1 - $13.80 \pm 7.52\%$ vs. Group 2 - $22.54 \pm 9.85\%$, $p < 0.0001$).

Comparison of the transmural index with hs-CRP plasma levels, determined on Day 5, revealed a significantly higher index among patients with persistent inflammatory status compared to those with low levels of hs-CRP, both from the point of view of the mass of the myocardial scar (Group 1 - 7.67g vs. Group 2 - 23.42g , $p = 0.04$) and volumetric (7.3ml versus 22.26ml , $p = 0.04$), this fact demonstrating a better correlation of hs-CRP determined on day 5 of the transmural extension of the infarct area, compared to the values determined on day 1.

Sub-study 2 tracked the impact of inflammatory median response on ventricular remodeling in the post-infarction period.

Patients with baseline increased inflammatory status presented lower FEVS values, measured by echocardiography on the 7th post-infarction day, compared to patients with a low level of hs-CRP in the first study group (Group 2 - $52.42 \pm 10.08\%$ vs. Group 1 - $59.75 \pm 7.41\%$, $p = 0.05$). Speckle tracking echocardiography performed on day 7 post-infarction identified significantly lower GLS values among patients with elevated levels of hs-CRP compared to subjects in the first group (Group 1: $-16.33 \pm 1.5\%$ vs. Group 2: $13.23 \pm 2.35\%$, $p = 0.006$), indicating more pronounced alteration of myocardial kinetics in patients with more exacerbated inflammatory status. This observation was also confirmed by the linear regression analysis of the correlation between the peak values of hs-CRP and the baseline GLS values. Moreover, the statistical analysis of data revealed the presence of a statistically significant positive correlation between the maximum serum hs-CRP and GLS, determined on day 7 ($r = 0.5395$, $p = 0.006$).

The determined post-infarction GLS value also showed a statistically significant positive correlation with the maximal serum hs-CRP quantitated on day 7 of post-infarction ($r = 0.5813$, $p = 0.002$).

At the same time, the group of patients with an altered inflammatory status exhibited a higher transmural extension of the infarct area with double values of the transmural index (g) compared to patients with low plasma levels of hs-CRP (Group 1 - $10.48 \pm 8.45\text{g}$ versus Group 2 - $25.55 \pm 15.11\text{g}$, $p = 0.006$).

Discussions and conclusions

Compared to the inflammatory response in the first 24h post-infarction, the persistence of an evolving inflammatory status is a more accurate marker for the extension of the impact of the myocardial ischemic process, quantified 1 month after the acute MRI event.

Baseline plasma IL-6 levels as a marker of inflammatory status showed a progressive increase associated with the extent of the infarct extension, constituting a biomarker of the impact of the ischemic process on the myocardium. Hs-CRP as an inflammatory biomarker for the screening of patients at risk of developing VS remodeling can bring a benefit with a particularly important clinical impact, allowing for more aggressive therapeutic management among these patients.

This study demonstrates that screening by complex paraclinical and imaging MRI methods allows stratification of vulnerable patients at high risk of developing major cardiovascular events.