Study of Serum Biomarkers in Heart Failure

PhD student: Buicu (Chiotoroiu) Andreea

Coordinator: Prof. Dr. Theodora Benedek

Introduction: Heart Failure is a major healthcare issue, affecting approximately 26 million people worldwide, while in Romania there are annualy 44.000 new cases diagnosed with heart failure. A significant proportion of patients with Heart Failure are caused by coronary artery disease, since myocardial infarction frequently leads to ventricular dysfunction. Identification of new biomarkers to characterise inflammatory status and ventricular dysfunction, as well as the instability degree of atheromatous plaques, which is directly linked with the further risk of recurrent cardiovascular events, would be extremely important for a proper monitorization of ventricular function in the post infarction period.

The aim of the research was to ellucidate the role of several serum biomarkers which express the systemic inflammatory status, ventricular function and atherogenic risk, for early detection of the postinfarction patient who is at risk for developping heart failure.

Methodology: This doctoral research took place in the interval 1 January 2017 – 31 December 2020, enrolling 123 patients in study 1 and 266 patients in study 2, addmited for acute coronary syndromes in the Intensive Coronary Care Unit of the Clinic of Cardiology in the County Clinical Emergency Hospital Tirgu Mures, Romania, a level 3 unit of intensive cardiac care.

Results:

Study 1: Study of correlation between biomarkers of ventricular dysfunction and inflammatory biomarkers in patients with acute myocardial infarction (AMI).

The objective of this study was to investigate the correlations between serum biomarers which express the severity of left ventricular dysfunction postinfarction and the serum biomarkers that express inflammatory status in AMI patients, in the immediate postinfarction phase.

Serum levels of NT-proBNP was determined in all patients, and according to its median value the patient population was divided into 2 groups: Group 1 includes 92 patients with NT pro-BNP levels below 3000 pg/mL, respectively Group 2 includes 31 patients with NT pro BNP levels above 3000 pg/mL. Serum levels of necrosis biomarkers (peak CK) was significantly higher in patients from group 2 (2.896 +/- 6.074 versus 940.6 +/- 892.6, p=0,003). Inflammatory biomarkers presented significantly higher levels in patients with ventricular dysfunction, as regards to hsCRP (12.3±8.9 versus 3.6±6.7, p<0,0001), and interleukin 6 (27.6 +/- 30.7 versus 8.6 +/- 6.2, p<0.0001). The long term impact of ventricular dysfunction on major cardiovascular eventrs was obviated by a significantly higher rate of major cardiovascular events, 1-year rehospitalization rate and deaths in the group with high NT-ProBNP (13.33% versus 8.7% for MACE, 12.9% versus 7.6% for re-hospitalization, respectively 6,4% vs 2,17% for deaths).

Study 2: Study of inflammatory biomarkers in patients with heart failuyre and acute coronary syndrome

The objective of study 2 was to investigate the association between inflammatory biomarkers and the type of acute coronary syndrome (unstable angina, NSTEMI or STEMI) in

patients presenting associated ventricular dysfunction.

The inclusion criteria were: high NT-proBNP levels, with a cut-off established at 300 pg/ml for patients in sinus rhythm, respectively at 900 pg/ml in patients with atrial fibrillation, or left ventricular ejection fraction below 45%, as assessed by echocardiography or cardiac MRI.

The average level of hsCRP was 4.9 +/- 4.5 in patients with unstable angina, compared to 20.4 +/- 42.2 in those with myocardial infarction, while interleukin 6 was 7.1 +/- 13.8 compared to 31.6 +/- 129.2 in those with myocardial infarction (p=0.001 for hsCRP respectively <0.0001 for interleukin 6). Îadhesion mollecules I-CAM și V-CAM did not exhibit any significant difference between the group with unstable angina and those with myocardial infarction, in patients with heart failure. Average value for IL-6 was 32.2 +/- 16.8 in STEMI patients, compared to 23.5 +/- 47.3 in other types of acute coronary syndromes. At the same time, I-CAM seems to have a higher discrimination power between STEMI and other forms of acute coronary syndromes in patients with heart failure, beiong more than double in STEMI patients (216.1 +/- 149.6 versus 448.2 +/- 754.4, p<0,0001).

In conclusion, the present research demonstrated that both pre-existing inflammatory status and the inflammation exarcebated by the acute event have a significant contribution to development of left ventricular dysfunction post myocardial infarction. Serum biomarkers that express the ventricular dysfunction (NT-proBNP, respectively BNP) present a significant contribution not only with the inflammatory status but also with the haemodynamic status in the acute phase and with the severity of coronary lesions. From all the inflammatory biomarkers, hsCRP, IL-6 and E-selectina correlate best with the biomarkers expressing the degree of ventricular dysfunction in patients with myocardial infarction. However, inflammatory biomarkers do not seem to be correlated with the type of infarction (STEMI or NSTEMI) or with the type of acute coronary syndrome (unstable angina or infarction). Adhesion mollecules, which reflect endothelial function, are not directly associated with ventriocular dysfunction, but present signficantly higehr value in STEMI patients. These observations indicate a potential predominant role of endothelial alterations in triggering an acute coronary event, especially when they are associated with an increased inflammation associated with heart failure. All these date indicate a more expressed contribution of systemic inflammation than of the local one, on the post-infarction evolution and progression towards heart failure, while local changes at the level of coronary endothelium seem to be more associated with the type of acute coronary syndrome.