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In search for novel prognostic markers for coronary artery disease

M. Popescu¹; CS. Stancu²; D. Deleanu²; L. Niculescu²; N. Simionescu²; A. Vlad³; AC. Popescu¹; D. Dimulescu¹; AV. Sima²

¹Elias Emergency University Hospital, Bucharest, Romania; ²Institute of Cellular Biology & Pathology Nicolae Simionescu, Bucharest, Romania; ³University of Medicine and Pharmacy Carol Davila, Bucharest, Romania

Purpose: Searching for new biomarkers to predict the progress of coronary artery disease (CAD), we studied the evolution of lipid and inflammatory parameters, along with five mi-RNAs, in plasma of CAD patients under treatment for 1 year.

Methods: Subjects were assigned to 5 groups: healthy subjects (C, 10), subjects with risk factors (RF, 10), stable angina (SA, 22), unstable angina (UA, 21) and 1 month post myocardial infarction (MI, 11) patients. Blood was collected at inclusion and after 1 year of standard treatment. We selected five miRNA (miR-92a, miR486a, miR-125a, miR-146a, miR-33a), due to their implication in lipid metabolism, cardiomyocytes and endothelial dysfunction. Lipid parameters were measured in plasma and serum, such as total cholesterol, triglycerides, phospholipids, LDL-C, HDL-C, and oxidative stress markers, such as oxidized LDL, 4-hydroxynonenal (4-HNE), 15(S)-hydroxy-eicosatetraenoic acid, 13(S)-hydroxyoctadecadienoic levels and paraoxonase-1(PON-1) activity. IL-1 β , CRP, matrix metalloproteinases (MMP-9, MMP-14) and soluble vascular adhesion protein (sVAP-1) were determined as

inflammatory markers. The statistical correlation between biochemical and clinical parameters was performed.

Results: After 1-year of treatment, our evaluation showed a significant improvement of the plasma lipid profile, decrease of the oxidative (lower plasma 4-HNE levels and increased serum PON1 activity) and inflammatory stress (lower IL-1 β levels and MMP-9 activity). Interestingly, IL-1 β levels were increased in sera from SA and UA patients under 60 compared to those over 60. Also, MMP-14 levels were increased in UA and decreased in MI sera from patients under 60 compared to those over 60. Levels of sVAP-1 were increased in MI (406.9 ± 72.34) compared to UA (348.29 ± 50.52 , $p < 0.05$) patients plasma. Plasma sVAP-1 levels were significantly increased in all diabetic versus non diabetic patients ($p < 0.05$). Circulating miR-486a and miR-92a levels were increased in MI compared to UA sera. All miRs levels were increased in UA patients under 60 compared to those over 60. Conclusions. As a consequence of the standard treatment administered, the lipid profile after 1 year suffered a definite improvement compared to baseline. The decrease of IL-1 β levels and MMP-9 activity in all patients' sera after one year treatment suggests that they might be adequate CAD markers. The increased levels of sVAP-1 in diabetic and post myocardial infarction patients indicate that this molecule could be a predictive marker for CAD evolution. The role of miRs as prognostic markers remains still under debate.