

Lipoprotein and Lipid profile can predict the disease activity in Rheumatoid Arthritis

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Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic and systemic synovial inflammation, cartilage erosion and subsequent joint destruction. Despite the existence of many targeted therapies, RA remains a disease with high morbidity, requiring monitoring with prognostic biomarkers. RA presents with abnormal lipoprotein levels, a phenomenon known as the “lipid paradox”, which requires comprehensive characterization with -omics techniques. The purpose of this study is to describe the distinct lipoprotein and lipidomic profile in active and remission RA populations, to globally map the effect of inflammation and disease activity on the metabolome and obtain biomarkers with predictive capacity.

Plasma samples of 161 RA patients were collected under fasting conditions. Patients were classified based on the disease activity score, DAS28, as High, Moderate, Low or Remission. Lipoproteins and their subclasses (n=112) were quantified using ¹H NMR spectroscopy with the B.I.LISA method (Bruker), while lipid species detection was achieved with mass spectrometry (DMS-MS) using the Lipidizer method (Sciex). Glycoproteins signals were acquired from ¹H NMR led spectra. High Disease Activity (n=21) and Remission (n=33) were analyzed pairwise with Multivariate (OPLS-DA) and univariate (t-test) methods. The correlation coefficient was calculated for the entire lipoprotein and lipid profiles with DAS28 for each group.

Patients with High activity showed relatively increased levels of VLDL, IDL, total Triglycerides, Free fatty acids (FFA(18:1), FFA(16:0)) and Phosphatidylcholines (PC(16:0/20:4), PC(18:0/20:4)) compared to Remission. RA patients in Remission were characterized by elevated LDL (LDPN, L4PN), HDL Apolipoprotein A1 (HDA1, H4A1), Cholesterol Esters (CE(18:2), CE(18:1)) and Phosphatidylcholines (PC(16:0/18:2), PC(18:0/18:2)). The entire lipoprotein and lipid profiles were correlated with DAS28 in Remission ($R^2=0.24$; $R^2=0.40$) and High disease activity ($R^2=0.26$; $R^2=0.47$) groups, indicating that the lipid profile is more predictive of the disease activity in both groups. Univariate analysis highlighted relatively higher concentration of large density HDL-4 subclasses (HDL-4 -Cholesterol ($p=0.0003$), ApoA1 ($p=0.0003$), ApoA2 ($p=0.0018$) and Phospholipids ($p=0.0024$)), Sphingomyelin (SM(24:0); $p=0.0012$), Hexosylceramide (HCER(22:0); $p=0.0057$), and Cholesterol Esters (CE(18:0); $p=0.0025$, CE(18:2); $p=0.0121$), but lower Glycoprotein A and B ($p=0.0003$; 0.0007) levels in Remission.

In summary, comprehensive lipoprotein and lipid analysis identifies markers that characterize RA in exacerbation and remission. Large density HDL-4 ApoA1 and CEs are indicative of Remission, while VLDL, TGs and FFAs describe active RA. The above markers will be evaluated in comparison with those already existing in clinical laboratory application

