However, this lack of association was due to the similarity of negative and low-positive patients, because the high-positive patients showed significant decrease of BMD at LS ($\beta = -0.39$, $p = 0.01$) and TH ($\beta = -0.30$, $p = 0.02$). Nevertheless, we did not found significant association at the juxta-articular bone of the MCP joints. Given the overlap between anti-CarPA and ACPA, we included the two autoantibodies in multivariate analysis. The association with BMD was significant only in the ACPA positive/anti-CarPA high-positive subgroup at LS and TH ($p = 0.007$ and 0.005 , respectively). In addition, the coefficients of regression were similar between the ACPA positive/anti-CarPA high-positive and the ACPA negative/anti-CarPA high-positive subgroups ($\beta = -0.50$ vs. -0.52 at LS, and $\beta = -0.37$ vs. -0.30 at TH).

Conclusions: We found significantly lower BMD at LS and TH in the patients with high anti-CarPA titers. These associations seem to be independent from the presence of ACPA, suggesting that anti-CarPA could contribute to systemic bone loss in EA patients.

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THU0068 IDENTIFICATION AND VERIFICATION OF BIOMARKER CANDIDATES FOR MONITORING RHEUMATOID ARTHRITIS ACTIVITY BY MASS SPECTROMETRY

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Background: Rheumatoid arthritis (RA) is a long-lasting inflammatory autoimmune disorder that ultimately leads to the destruction of joint architecture. The activity of this disease is measured by the assessment of clinical symptoms.

Objectives: To apply a proteomic strategy to find serum biomarkers able to discriminate patients with different RA activities.

Methods: To facilitate the complex measurement of serum by proteomics, a simple, fast and reproducible albumin-specific depletion method using ethanol was optimised and applied to the samples employed in this study. 80 samples from the IMID consortium, classified according to the DAS28 score into low activity⁴⁰ and high activity⁴⁰ were analysed by mass spectrometry. Four independent pools of the high RA activity samples (10 samples per pool) and 4 pools of the low RA activity samples were firstly albumin-depleted, and then the remnant serum proteins were digested and differentially labelled with iTRAQ 8-plex reagents. Subsequently, the 8 labelled pools were combined and cleaned using StageTips-C18. Finally, the pool mixture was fractionated by HPLC (Zorbax-C18) and the resulting fractions were analysed by nanoLC-MS/MS using MALDI-TOF/TOF, TripleTOF and LTQ-Orbitrap.

Results: The mass spectrometry analysis led to the identification of 186 proteins. In this screening step, the abundance of 9 proteins was found to be significantly different between patients with high (H) and low (L) RA activity. Orthogonal experiments, using Western Blot, protein bead arrays and Multiple Reaction Monitoring (MRM) with synthetic heavy-labelled peptides, were conducted in order to verify some of these biomarker candidates of RA activity. The results obtained from the verification phase, conducted by MRM on 50 samples from the same cohort, show a decrease of Apolipoprotein B (ratio H/L=0.84, $p = 0.00$), Histidine Rich Glycoprotein (ratio H/L=0.86, $p = 0.01$) and Plasma protease C1 inhibitor (ratio H/L=0.84, $p = 0.02$). Furthermore, this verification phase shows also an increase of Haptoglobin (ratio H/L=1.34, $p = 0.01$) and Serum Amyloid A1 (ratio H/L=1.64, $p = 0.05$), in accordance with that observed in the screening. These proteins are related with the RA process and the effects caused by this type of disease (inflammation and immune disorder in joints).

Conclusions: In this proteomic study, 5 proteins were found to be quantitatively altered between patients with high and low RA activity using shotgun and targeted mass spectrometry.

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THU0069

IN RA, BECOMING SERONEGATIVE OVER THE 1ST YEAR OF DMARD TREATMENT DOES NOT TRANSLATE TO BETTER CHANCES OF SUSTAINED DRUG-FREE REMISSION IN THE LONG-TERM

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Background: In rheumatoid arthritis (RA), autoantibodies are a reflection of the underlying B cell autoimmunity and an important predictor of long-term outcome. Baseline seropositivity is a poor prognostic factor for sustained drug-free remission (SDFR). However, autoantibody levels may change and patients may become seronegative under treatment. It is unknown how often this happens and whether some autoantibodies (depending on isotype use or antigen recognition) disappear more often than others. Furthermore, it is unclear whether becoming seronegative early in disease, indicating disappearance of serological autoimmunity, improves chances of SDFR.

Objectives: To longitudinally characterise the levels and presence of autoantibodies in RA patients and to investigate whether changes in these levels and/or presence associates with SDFR.

Methods: In sera of 399 seropositive RA patients in the IMPROVED study¹, we measured, at 4-month-intervals over the first year of treatment: IgG, IgM, and IgA isotypes for anti-cyclic citrullinated peptide-2 (anti-CCP2) and anti-carbamylated protein antibodies (anti-CarP), IgM and IgA for rheumatoid factor (RF), and IgG autoantibodies against 4 citrullinated and 2 acetylated peptides. We investigated whether changes in antibody levels and seroconversion from positive to negative for each individual antibody was favourable for SDFR (drug-free DAS44 <1.6 lasting ≥ 1 year until last follow-up).

Results: For all 14 antibodies, median levels decreased significantly between baseline and 4 months and then stabilised. Most seroconversion to negative happened within the first 4 months of treatment (with prednisone and methotrexate), after which some patients converted back to seropositive. The prevalence of seroconversion varied substantially depending on the autoantibody. The percentage of patients who were seropositive at baseline and became seronegative by 12 months varied substantially depending on the autoantibody: 2% (anti-CCP2 IgG) to 66% (anti-CarP IgA) (see figure 1). We hypothesised that greater level decreases and seroconversion to negative might be favourable for the long-term outcome SDFR, but surprisingly, greater median decreases in levels were not associated with higher chance of SDFR for any antibody. Furthermore, using Chi-squared tests, we found no evidence that rates of SDFR were higher in patients who seroconverted to negative compared to those who stayed seropositive, for any of the 14 antibodies analysed (see figure 1).

Abstract THU0069 – Figure 1. Percentage of patients reaching SDFR (drug-free DAS44 <1.6 lasting ≥ 1 year until last follow-up), separated by whether patients