Conclusion: This trial is the first to report that MRI tenosynovitis independently predicts both X-ray and MRI damage progression in RA patients in clinical remission. Further studies are needed to confirm MRI-determined tenosynovitis as predictor of progressive joint destruction in RA clinical remission.

REFERENCES:
[2] Möller-Bisgaard et al. JAMA, accepted Dec 2018

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Novel autoantibodies in RMD: a reovering quest?

OP0333 RISING ACPA IGG VARIABLE DOMAIN GLYCOSYLATION PRE-DISEASE ASSOCIATES WITH AN INCREASE IN AUTOANTIBODY LEVELS AND THE DEVELOPMENT OF RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein antibodies (ACPAs) are present in the majority of rheumatoid arthritis (RA) patients (60-70%) and play a pivotal role in disease development. ACPAs are unique in a way that they are abundantly N-glycosylated within their variable regions. These variable domain (V-domain) glycans can be found on over 90% of ACPAs present in sera from RA-patients. To under no N-linked glycosylation, a consensus sequence in the protein backbone is required. In our study, we found the N-linked glyco- sylation sites in ACPA-IgG V-domains are introduced during somatic hypermutation and that the introduction of such sites likely conveys a selective advantage to ACPA expressing B-cells. However, it is currently unknown, whether ACPA-expressing B-cells already introduced glycosylation-sites into their V-domains before disease onset or when ACPA-V-domain glycosylation occurs.

Objectives: To investigate the appearance of ACPA V-domain glycosylation in pre-symptomatic individuals and RA patients.

Methods: In a case-control study, individuals (n=201) from the Medical Biobank, who were sampled before onset of symptoms (mean±SEM predating time; 5.8 ±0.3 years) (140 ACP+ and 61 aCP-), and after diagnosis of RA (n=99, 94 aCP+ and 5 aCP-) and randomly selected control samples (n=43, 3 aCP+ and 40 aCP-) were analyzed for their ACPA IgG V-domain glycosylation levels. ACPA IgGs were affinity purified, N-linked glycans released, and 2-AA labeled for further analysis using UHPLC. Data calibration and integration was performed and a cut-off defined. Samples below the cut-off were determined as non-detectable and excluded from the analysis. The percentage V-domain glycosylation was calculated as described previously.

Results: Our data indicated that ACPA IgG V-domain glycans are already present years before symptom onset, in pre-symptomatic individuals who subsequently will develop RA. Analysis of matched pairs showed a significant increase of ACPA V-domain glycosylation in RA patients compared to individuals pre-dis- ease (p<0.001). The results showed that ACPA N-glycosylation was correlated with anti-CP concentrations pre-disease (r = -0.504, p<0.001), while no such association can be found after RA onset. Further, V-domain glycosylation increases closer to symptom onset.

Disclosure of Interests: None declared