SAT0037

HIGH AGREEMENT BETWEEN ANTIBODIES AGAINST MALONDIALDEHYDE PROTEIN ADDUCTS AND ANTIBODIES AGAINST MALONDIALDEHYDE-ACETALDEHYDE ADDUCTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) presents high levels of oxidative stress and reactive species such as malondialdehyde, which modifies proteins forming malondialdehyde adducts (MaP) and, in the presence of acetaldehyde generates adducts called malondialdehyde-acetaldehyde (MaaP). Recently, the presence of malondialdehyde modified proteins in the synovium and antibodies against these adducts (AMaPA) in the serum of patients with RA has been described (1). Previously, a high frequency of antibodies against MaaP (AMaaPA) had been reported in patients with RA (2).

Objectives: We aimed to confirm the presence of AMaPA in patients with RA and define its relationship with AMaaPA.

Methods: The sera of 204 healthy controls and 205 patients with established RA that met the 1987 ACR classification criteria and selected to represent the different AMaaPA status were studied. All had information on their status for RF, anti-CCP and AMaaPA antibodies (IgG, IgM and IgA). The AMaPA were determined by indirect ELISA using malondialdehyde-modified serum bovine albumin as antigen and specific secondary antibodies against the IgG and IgM isotypes following the same protocol of the previous study (1). The results were analyzed with the gamma coefficient (γ) for concordance in status and with the Spearman coefficient (ρ) for correlation of titres. The study was approved by the CEIC of Galicia.

Results: The AMaPA showed higher titres in the patients with RA than in the controls, the positive frequencies being: 17.1% for IgG AMaPA and 25.4% for IgM AMaPA. An important fraction of the patients with RA showed the same status with the two AMaPA isotypes, as reflected in the significant concordance between them ($\gamma = 0.74$, Table 1). When comparing the AMaPA and AMaaPA status in patients with RA, a remarkable concordance was observed among the antibodies of the same isotype, especially between the IgM AMaPA and IgM AMaaPA: $\gamma = 0.83$ (Table 1). There were fewer patients with the same status when different antibody isotypes were compared, although some of these comparisons reached statistically significant concordance. However, the titres were not significantly correlated in any of the comparisons, even in those that showed the greatest agreement in status (Table 1).

Table 1. Relationship of antibodies against malondialdehyde adducts (AMaPA) with other autoantibodies in patients with RA.

AMaPA	2nd antibody	γ	P	ρ	P
IgG	IgM AMaPA	0.74	1.5E-14	0.23	0.3
IgM	IgM AMaaPA	0.83	3.4E-25	0.26	0.1
IgG	IgG AMaaPA	0.65	2.4E-08	0.11	0.7
IgM	IgA AMaaPA	0.42	0.0017	0.26	0.4
IgG	IgM AMaaPA	0.39	0.00096	0.08	0.8
IgG	IgA AMaaPA	0.21	0.2	-0.09	0.9
IgM	IgG AMaaPA	0.16	0.3	0.13	0.7
IgM	RF	0.48	0.000011	na	na
IgM	Anti-CCP	0.39	0.00076	-0.34	0.031
IgG	Anti-CCP	0.05	0.7	-0.18	0.4
IgG	RF	0.02	0.9	na	na

In relation to the typical RA autoantibodies, significant concordances were observed between the IgM AMaPA and RF or anti-CCP, although they were lower than those observed with the AMaaPA. In contrast, the IgG AMaPA showed no significant agreement with RF or anti-CCP antibodies. These low levels of concordance were reflected in the lack of significant difference in the prevalence of AMaPA between seronegative and seropositive patients (24.1% vs. 35.4%, $P = 0.1$).

Conclusion: The presence of AMaPA in patients with RA has been confirmed, and a high concordance between the AMaPA and AMaaPA status has been observed, especially between those with an IgM isotype. However, the lack of correlation in the titres indicates that these two types of autoantibodies are independent. The potential utility as biomarkers of the AMaPA should be similar to that of the AMaaPA.

References:

- [1] Grönwall C, et al. J Autoimmun. 2017, 84:29-45
- [2] Thiele GM, et al. Arthritis Rheumatol. 2015, 67:645-55

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SAT0038

CHANGES IN ILLNESS PERCEPTIONS IN PEOPLE WITH RHEUMATOID ARTHRITIS OVER THE FIRST YEAR OF TREATMENT WITH METHOTREXATE

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Background: Illness perceptions at treatment onset are known to be important predictors of treatment response in rheumatoid arthritis (RA). Yet it is unknown how these perceptions change over time after the initiation of treatment, or which factors are associated with changing perceptions.

Objectives: To identify groups of patients with early RA who have similar changes in illness perceptions over the first year following treatment, and assess predictors of these changes.

Methods: Patients starting methotrexate (MTX) for the first time were recruited to the Rheumatoid Arthritis Medication Study (RAMS), a one-year prospective cohort. The DAS28 was calculated and patients completed a questionnaire at baseline and 12 months, reporting demographics and completing the HAQ, the Hospital Anxiety and Depression Scale (HADS), pain and fatigue visual analogue scales (VAS) and the Brief Illness Perception Questionnaire (B-IPQ). The B-IPQ consists of eight Likert scales: five represent cognitive illness perceptions (B-IPQ1-5), two represent emotional representations (B-IPQ6 & 8) and one represents illness comprehensibility (B-IPQ7). Change in illness perceptions and EULAR response were calculated over 12 months in those with data at both timepoints. Latent profile analysis was used to identify profiles of patients with similar changes in illness perceptions. Candidate predictors of profile membership were assessed using logistic regression. The association between profile and EULAR response was assessed using ordered logistic regression.

Results: In total 1188 patients were included (mean [SD] age: 59.8 [12.7], 781 [65.7%] women). On average, illness perceptions for the whole cohort improved over 12 months, other than patients' perception of longevity of arthritis (B-IPQ2) and of treatment helpfulness (B-IPQ4). Three profiles were identified: Small Improvers (N=900), Small Deteriorators (N=78) and Large Improvers (N=210) (Figure). Small Improvers improved on all B-IPQ items other than their perception of longevity of arthritis (B-IPQ2) and of treatment helpfulness (B-IPQ4). All B-IPQ items improved in the Large Improvers group to a greater extent than the Small Improvers, other than arthritis longevity (B-IPQ2). The perceptions of Small Deteriorators all worsened, other than arthritis comprehensibility (B-IPQ7). Higher baseline pain was associated with greater odds of being in both the Small Deteriorators and Large Improvers compared to Small Improvers (Small Deteriorators: OR 1.56 per standard deviation (SD) increase in pain [95% CI 1.11, 2.18]; Large Improvers: OR 1.46 per SD increase in pain [95% CI 1.15, 1.85]). Odds of better EULAR response were greater in the Large Improvers (OR 4.37 [95% CI 3.01, 6.33]) and worse in the Small Deteriorators (OR 0.50 [95% CI 0.29, 0.87]) compared to Small Improvers.

Conclusion: In general, illness perceptions improved over the first year of MTX treatment and improvements were associated with better treatment response. Worsening illness perceptions may be driven by poor treatment response. These poor illness perceptions at follow-up may compound poor treatment response in the future. Greater understanding of patients' initial and subsequent illness perceptions is crucial, given the association with treatment response.

Figure:

Figure – Illness Perception Questionnaire items over 12 months, stratified by the latent profiles [10 represents worst illness perception]

B-IPQ1: How much does arthritis affect your life?
 B-IPQ2: How long do you think your arthritis will continue?
 B-IPQ3: How much control do you feel you have over your arthritis? (reverse coded)
 B-IPQ4: How much do you think your treatment can help your arthritis? (reverse coded)
 B-IPQ5: How much do you experience symptoms from your illness? (reverse coded)
 B-IPQ6: How concerned are you about your arthritis?
 B-IPQ7: How well do you feel you understand your arthritis? (reverse coded)
 B-IPQ8: How much does your arthritis affect you emotionally?

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SAT0039

ADAPTIVE DEEP LEARNING FOR THE PREDICTION OF INDIVIDUAL DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) lacks reliable biomarkers that predict disease evolution on an individual basis, potentially leading to over- and under-treatment. Deep neural networks learn from former experiences on a large scale and can be used to predict future events as a potential tool for personalized clinical assistance.

Objectives: To investigate deep learning for the prediction of individual disease activity in RA.

Methods: Demographic and disease characteristics from over 9500 patients with 65.000 visits from the Swiss Quality Management (SCQM) database were used to train and evaluate an adaptive recurrent neural network (AdaptiveNet). Patient and disease characteristics along with clinical and patient reported outcomes, laboratory values and medication were used as input features. DAS28-BSR was used to predict active disease and future numeric individual disease activity by classification and regression, respectively.

Results: AdaptiveNet predicted active disease defined as DAS28-BSR>2.6 at the next visit, with an overall accuracy of 75.6% and a sensitivity and specificity

of 84.2% and 61.5%, respectively. Apart from DAS28-BSR, the most influential characteristics to predict disease activity were joint pain, disease duration, age and medication. Longer disease duration, age >50 or antibody positivity marginally improved prediction performance. Regression allowed forecasting individual DAS28-BSR values with a mean squared error of 0.9.

Conclusion: Deep neural networks have the capacity to predict individual disease outcome in RA. Low specificity remains challenging and might benefit from alternative input data or outcome targets.

References:

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Figure 1. Examples of true disease activity and corresponding predictions of AdaptiveNet by regression analysis. Predictions are made step to step from the current to next visit.

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SAT0040

RISK FACTORS FOR DEVELOPING AND MORTALITY FOR ACUTE EXACERBATION OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Among collagen vascular diseases, rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is the most commonly associated with ILD with acute exacerbation (AE) [1]. One study reported that ILD diagnosis at an older age, the usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography, and methotrexate (MTX) use were associated with AE in patients with RA-ILD [2]. However, because these studies included few patients, the risk factors and prognosis of AE in patients with RA-ILD remain unclear.