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FRI0042

DISCREPANCIES BETWEEN RAPID3 AND DAS28 IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION OR LOW DISEASE ACTIVITY RECEIVING TNF INHIBITORS: WHAT IS THE ROLE OF THE INFLAMMATION BIOMARKERS?

J. Inciarte-Mundo¹, R. Morlà¹, B. Frade-Sosa¹, J. Ramírez¹, R. Castellanos-Moreira¹, V. Ruiz¹, J. D. D. Cañete¹, J. Gomez Puerta¹, R. Sanmartí¹. ¹Hospital Clínic de Barcelona, Rheumatology Department, Barcelona, Spain

Background: Patients and Rheumatologist often differ in their perception of RA disease activity. Remission or low disease activity should be the treatment target in RA, patients should be included in treatment decisions.

Objectives: To identify factors influencing patient's self-reported disease activity by RAPID3 test.

Methods: 47 RA patients in remission or low disease activity by DAS28ESR (DAS28ESR ≤ 3.2) receiving TNFi (etanercept, adalimumab and infliximab) stratified their disease activity by RAPID3, then two patients' groups were defined: *target group* (RAPID3 with remission 0-3 or low disease activity 3.1-6), *non-target group* (RAPID3 with moderate 6.1-12 or high disease activity >12). Demographic data, disease duration, autoantibody status, radiological data, concomitant csDMARD therapy was collected. Laboratory measurements included CRP, ESR, calprotectin serum levels, TNFi trough serum levels, and antidrug antibodies (enzyme-linked immunosorbent assay (ELISA) test kit (Calprolab™ Calpro AS, Oslo, Norway, and Promonitor®, Progenika SA, Spain, respectively) according to the manufacturers' protocol. Pearson's correlations coefficients were used to identify variables correlating with RAPID3 score. Mixed-effects analyses of covariance (ANCOVAs) models were used to identify factors influencing RAPID3 score.

Results: Patients in "target group" have shown a significant lower TJC, pain by VAS 0-10mm, and calprotectin serum levels, but higher TNFi serum trough levels in comparison to "non-target group". When patients were classified according to RAPID3 categories, patients in "remission" have shown lower calprotectin serum levels than those classified as in "high disease activity" (0.94 (4.88-0.14) vs. 4.57 (7.97-1.25), $p=0.001$, respectively). Accordingly, when classified according to pain by VAS 0-10mm, patients with low levels of pain had lower calprotectin serum levels vs. those with severe pain (1.43 (6.33-10.14) vs. 5.16 (8.80-1.25), $p=0.009$, respectively). When distributed according to PGA (1=very good, 2=good, 3=regular, 4=bad, 5=very bad) patients in "very good" group had lower mean of calprotectin serum levels than those in "very bad" group (0.94 (4.88-0.14) vs. 4.57 (7.97-1.25), $p=0.001$, respectively). PGA and Pain VAS have shown a strong correlation with RAPID3 (R^2 0.978, and 0.834, $p=0.001$, respectively), while calprotectin and TNFi serum trough levels showed a moderate correlation (R^2 0.311, and 0.372, $p=0.005$, respectively). The multivariate adjusted analysis showed a significant association between Pain and RAPID3 ($p<0.001$) according to the different covariates (age, gender, anti-CCP positivity, time in remission, SJC, TJC, DAS28ESR). In addition, calprotectin and TNFi trough serum levels were associated with RAPID3 ($p<0.005$). Backward selection of variables did not substantially modify the association between RAPID3 and pain, calprotectin and TNFi trough serum levels.

Conclusion: 61.7% of RA patients undergoing TNFi classified as in remission or low disease activity by DAS28ESR, self-reported their disease activity as moderate or high by RAPID3. The most significant factor influencing patient's perception of disease activity is pain (pain VAS and TJC). However, inflammation markers (calprotectin, TNFi serum trough levels) remain statistically significant after fully adjustment by different confounders. Thus, therapies improving these three domains will have a larger impact in patient's perception of disease activity.

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FRI0043

JOINT SPACE NARROWING PRECEDES EROSIVE RADIOGRAPHIC DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Kerschbaumer¹, F. Alasti¹, G. Supp¹, J. S. Smolen¹, D. Aletaha¹. ¹Medical University of Vienna, Department of Medicine III, Division of Rheumatology, Vienna, Austria

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized through symmetric polyarthritis leading to joint destruction over time in many patients. Radiographic damage is an important outcome in RA clinical trials, most commonly assessed by conventional radiographs and quantified/ reported by the modified total Sharp van der Heijde Score (mTSS). The mTSS is assessing erosive (ERO) changes as well as joint space narrowing (JSN; reflecting cartilage wasting) in the small joints of the hands and feet. While erosions are the hallmarks of RA, loss of cartilage has been reported to be highly relevant for functional limitations in RA. The sequence of occurrence of these events is not completely understood.

Objectives: To investigate the time to radiographic progression and assess potential differences between time-to-JSN progression and time-to-ERO progression.

Methods: Radiographs of RA patients from a large prospective clinical routine cohort were scored using the mTSS by one experienced reader (G.S.) unaware of the aim of this project. Time-to-JSN and time-to-ERO was estimated using survival analyses utilizing the Kaplan-Meier estimator. In additional analyses, patients were stratified based on JSN and/or ERO damage at baseline. Further, potential predictors (demographics, csDMARD/bDMARD treatment/combination therapy) of time-to-ERO and time-to-JSN were evaluated using Cox-regression techniques. All statistical analyses were conducted using SAS v9.4 (Cary, New York, USA).

Results: We assessed 798 patients longitudinally for radiographic progression. JSN occurred significantly earlier than erosions ($p<0.001$, Figure 1). After stratification for baseline damage (Figure 2), these differences remained significant with a shorter time-to-JSN in patients without any baseline ERO or JSN ($n=44$, $p=0.008$), patients with JSN but no ERO at baseline ($n=200$, $p<0.001$), and patients with baseline ERO and JSN ($n=536$, $p<0.001$). Only in the small group of patients with isolated erosions (without JSN) at baseline there was no difference in time-to-progression of ERO vs. JSN ($n=18$, $p=0.241$). Overall, shorter time to progression of ERO was significantly predicted by positivity for rheumatoid factor or anti-citrullinated peptide antibodies (CCP; $p<0.003$), as well as by erosions at baseline ($p<0.001$) in Cox regression. In contrast, seropositivity for neither RF nor CCP was associated with shorter time to JSN progression ($p=0.226$); however, baseline concomitant JSN and ERO damage did show to be a significant predictor ($p<0.001$).