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POS0485 **TRAJECTORY CLUSTERS OF RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS: ASSOCIATIONS WITH CLINICAL VARIABLES**

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Background: Joint damage is a defining feature of rheumatoid arthritis (RA), a major driver of functional impairment and of reduction of quality of life. Many factors are associated with damage accrual however, the course of structural damage of individual patients over time and factors associated with such trajectories have not been investigated.

Objectives: Identification of trajectories of radiographic damage in RA by clustering patients according to the shape of their curve of Sharp-van der Heijde scores (SHS) over time. Developing models to predict their progression cluster from baseline characteristics.

Methods: Patient-level data over a two-year period from 5 large randomized controlled trials on TNF-inhibitors in RA (ERA, PREMIER, TEMPO, GO-BEFORE and GO-FORWARD) were used. SHSs were clustered in a shape-respecting manner to identify distinct clusters of radiographic progression. Characteristics of patients within different progression clusters were compared at baseline and over time. Logistic regression models were developed to predict trajectory of radiographic progression using information at baseline.

Results: In total 1887 patients with 7738 x-rays were used for cluster analyses. We identified 4 distinct clusters with characteristic shapes of radiographic progression: one with a stable SHS over the whole 2-year period (C0/lowChange; 86%); one with relentless progression (C1/rise; 5.8%); one with decreasing SHS (C2/improvement; 6.9%); and one going up and down (C3/bothWays; 1.4%) of the SHS. Robustness of clusters and shapes of progression over time were confirmed using different clustering methods and cut-offs to define radiographic progression (Figure 1). Regression models identified disease duration, baseline CRP and SHS and treatment status as predictors for cluster assignment (Table 1), showing good performance (PCC 87.5%; Nagelkerke r^2 0.36).

Conclusion: We were able to identify 4 different clusters of radiographic progression over time in patients with RA, most remarkably one with relentless progression and another one with amelioration of joint damage over time, suggesting the existence of distinct patterns of joint damage accrual in RA. The nature of the

identified trajectories is mostly explained by inflammatory load, disease duration and especially type of treatment.

Table 1. Simple logistic regression models to predict assignment to clusters of radiologic progression using information at baseline. Variables entered but not selected by a stepwise approach were: rheumatoid factor, age, gender, tender joint count;

c0/low change vs:	C1/rise Cluster		C2/improve Cluster	
	OR	95%CI	OR	95%CI
X-ray Score	1.02	1.01-1.03	1.03	1.02-1.03
CRP (mg/dl)	1.12	1.07-1.16	0.98	0.90-1.07
Duration (years)	0.87	0.80-0.95	1.09	1.05-1.12
Treatment				
Combination	REF	REF	REF	REF
csDMARD	4.98	2.88-8.63	0.05	0.01-0.23
bDMARD Mono	2.28	1.29-4.04	0.64	0.38-1.08

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POS0486 **FACTORS ASSOCIATED WITH CHRONOTROPIC RESPONSE IN PEOPLE WITH RHEUMATOID ARTHRITIS**

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Background: People with rheumatoid arthritis (RA) are at high risk for cardiovascular diseases (CVD) and CVD mortality. Reduced Chronotropic response (CR), which produces exercise intolerance, is known as a contributing factor to CVD and mortality. Studies have shown that people with RA have reduced CR. However, knowledge about the factors associated with CR in people with RA is limited.

Objectives: To explore the factors associated with CR including CVD risk factors, inflammatory markers and cardiorespiratory fitness (VO_2 peak).

Methods: 106 people with RA completed a treadmill exercise tolerance test while heart rate (HR) was monitored via 12 leads ECG. CR was defined as the percentage of [(achieved peak HR minus resting HR) divided by (age-predicted maximum HR minus resting HR)]. Serological CVD risk factors and inflammatory markers including lipids profile, markers of insulin resistance and sensitivity (HOMA, QUICKi), high sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), fibrinogen and white blood cells (WBC) were examined via a fasted blood sample. VO_2 peak was assessed via breath-by-breath gas analysis.

Results: 34% had reduced CR based on the cut-off value ($\leq 80\%$) and the average CR was $86.2 \pm 21\%$. Body mass index ($r=-0.33$, $p=.001$), HOMA ($r=-0.26$, $p=.009$), hsCRP ($r=-0.23$, $p=.02$), ESR ($r=-0.21$, $p=.04$), fibrinogen ($r=-0.2$, $p=.05$), WBC ($r=-0.21$, $p=.04$) were inversely associated with CR, whereas, high density lipoprotein (HDL) ($r=0.43$, $p<.001$), QUICKi ($r=0.31$, $p=.002$), and VO_2 peak ($r=0.4$, $p<.001$) were positively associated with CR. When all the variables were entered into a stepwise linear regression, HDL ($p<.001$) and VO_2 peak ($p=.009$) were independently associated with CR.

Conclusion: The current findings suggest that CR in RA was associated with many CVD risk factors, inflammatory markers, and cardiorespiratory fitness. Among all the variables, HDL and cardiorespiratory fitness were moderately and independently associated with CR. Future studies should investigate the effect of improving these associated variables on CR in people with RA via exercise training programmes.

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Figure 1. Representations of the major three clusters of radiologic progression curves.(A) shows the curves of all patients with a SHS-range ≥ 10 , colored by their cluster. Values between visits were linearly interpolated. Big dotted line is the median of particular cluster, thinner lines represent single patient values. Cluster C0/lowChange are patients without enough variation in SHS to be seen as a curve, therefore not shown in the diagrams.

George Kitas from the University of Birmingham and Prof. George Metsios from the University of Wolverhampton.

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POS0487

ASSOCIATION OF RHEUMATOID ARTHRITIS WITH MORTALITY IN A COHORT OF CHRONIC KIDNEY DISEASE PATIENTS

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Background: Rheumatoid Arthritis (RA) is associated with an increased risk of cardiovascular disease. RA is also associated with increased risk of chronic kidney disease (CKD) (1, 2), which is a known cardiovascular risk factor (3). We hypothesized that RA (compared with no RA) would be associated with increased risk of mortality among a cohort of patients with CKD.

Objectives: To determine the risk of mortality in RA patients with CKD.

Methods: This study was conducted using participants from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) prospective Chronic Renal Insufficiency Cohort (CRIC) study. Approximately 3600 participants were enrolled from seven US clinical centers. Patients aged 21 – 74 years with mild to moderate CKD were eligible for enrollment. The primary outcome of interest was all-cause mortality. Secondary outcomes of interest included: kidney event defined as end stage renal disease (ESRD) or 50% decline in estimated glomerular filtration rate (eGFR), myocardial infarction (MI), cerebrovascular accident (CVA), heart failure and a composite cardiovascular endpoint. The association of RA mortality over time was examined using Cox multivariate proportional hazards regression, adjusting for potential covariates (age, sex, race/ethnicity, BMI, current smoker, education).

Results: The study cohort included 492 participants with self-reported RA with a mean follow up of 9.5 years. Compared to the non-RA group, RA patients tended to be older, female, Black. Hypertension, diabetes, use of prednisone was more prevalent among the RA cohort. The unadjusted hazards ratio (HR) for mortality based on RA status was 1.45 (1.26, 1.67) but this association was attenuated after adjusting for the confounding factors [aHR 1.09 (0.94, 1.27)] (Table 1). Participants with RA had a significantly higher risk for heart failure than those without RA [aHR 1.17 (1.02, 1.34)]. We did not observe a statistically significant association between RA status and other secondary outcomes.

Table 1. Estimated hazard ratios (HR) for various outcomes from Cox proportional hazards regression for RA status

	Unadjusted	Model 1	Model 2
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Death	1.45 (1.26, 1.67)	1.09 (0.94, 1.27)	1.13 (0.97, 1.32)
MI or death	1.43 (1.25, 1.63)	1.09 (0.95, 1.26)	1.15 (0.99, 1.33)
CVA or death	1.42 (1.24, 1.63)	1.07 (0.92, 1.24)	1.11 (0.95, 1.29)
CHF or death	1.54 (1.35, 1.75)	1.17 (1.02, 1.34)	1.22 (1.06, 1.40)
Composite	1.49 (1.31, 1.69)	1.13 (0.99, 1.30)	1.18 (1.03, 1.35)
Kidney event	1.09 (0.94, 1.27)	0.91 (0.78, 1.07)	1.01 (0.85, 1.20)

Model 1 adjusted for: age, sex, race/ethnicity, BMI, current smoker, education Model 2 adjusted for: model 1 + cardiovascular risk factors (urine albumin creatinine ratio, systolic blood pressure, estimated glomerular filtration rate)

Conclusion: RA was not associated with higher mortality among participants with CKD. However, RA was associated with higher rates of heart failure. Further studies evaluating the mechanisms behind this association are needed.

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POS0488

THE IMPACT OF ANTINUCLEAR ANTIBODIES INDUCED BY ANTI-TUMOUR NECROSIS FACTOR ALPHA AGENTS ON THE LONG-TERM TREATMENT OUTCOMES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: The seroconversion of antinuclear antibodies (ANA) induced by anti-tumour necrosis factor alpha (anti-TNF- α) therapy remains a matter of concern in various inflammatory conditions namely rheumatoid arthritis. However, evidence is still scarce regarding the impact of these autoantibodies on the clinical response to treatment in these patients.

Objectives: This study aimed to explore the impact of ANA induced by anti-TNF- α therapy on the outcomes of treatment in patients with rheumatoid arthritis over two years of follow-up.

Methods: An observational retrospective cohort study was conducted with two years of follow-up. Patients diagnosed with rheumatoid arthritis, according to the American College of Rheumatology (ACR) criteria, and registered on the Rheumatic Diseases Portuguese Register (Reuma.pt) who started their first anti-TNF α agent as first biologic between 2003 and 2018 were included. Patients with positive ANA (titer ≥ 100) and/or positive anti-double stranded DNA (anti-dsDNA) antibodies and/or with a diagnosis of SLE at their first visit were excluded. Demographic, clinical and laboratory data were obtained by consulting Reuma.pt. Disease Activity Score for 28 joints (DAS28), DAS28 delta, Health Assessment Questionnaire (HAQ), HAQ delta were assessed at baseline, 6, 12, 18 and 24 months. Clinical response was evaluated by EULAR criteria and three response categories were defined: good, mild and no response. The rate of switch of biological treatment was assessed over 24 months. To examine the differences between groups with and without ANA seroconversion independent samples t test for normally distributed continuous data, Mann-Whitney U-tests for non-normally distributed continuous data and Chi-square tests for categorical data were used. Logistic regression models were used to assess the effects of ANA seroconversion on clinical response to treatment

over 6, 12, 18 and 24 months.

Results: A total of 185 patients (mean age of 49.3 $\pm$ 10.9 years old; 85.4% female) with a median follow-up of 7 [4-14] years were included. We found an ANA seroconversion rate (titer ≥ 100) of 77.3% (n=143) with median time of 36 [15-72.3] months. There were no differences among groups regarding age, gender, disease duration, be seropositivity or not (for rheumatoid factor and/or anti-citrullinated protein antibodies) and have an erosive disease or not. DAS28 delta was significantly different (p=0.035) between group with positive ANA (2.01 $\pm$ 1.29) and negative ANA (1.15 $\pm$ 1.51) at 6 months. DAS28 was significantly different (p=0.014) between group with positive ANA (5.06 $\pm$ 3.39) and negative ANA (3.99 $\pm$ 1.43) at 12 months. No statistically significant differences were found in the DAS28, DAS28 delta, HAQ, HAQ delta at 18 and 24 months and in the EULAR response at any time. Switch rate was significantly different between patients with ANA seroconversion (median 1[0-1]) versus absence of seroconversion (median 0[0-1]), p=0.025. In the regression model ANA seroconversion did not predict switch rate and EULAR response over time.

Conclusion: This study showed that the majority of patients with rheumatoid arthritis treated with an anti-TNF- α agent developed ANA and that their presence may be associated with worse clinical results (DAS28) at 6 and 12 months. In fact, previous research suggested that a decrease in anti-TNF- α drug concentration due to the production of autoantibodies may lead to worse outcomes of treatment. Moreover, our data demonstrated that patients with ANA seroconversion