moderate to marked hyperemia (Power Doppler grade 2 and 3). Levels of sVCAM-1 ($r=0.20$, $p=0.028$), Tie-2 ($r=0.28$, $p=0.001$), and Angiostatin ($r=0.25$, $p=0.006$) correlated with a global arthritis sum score, defined by the sum of the semiquantitative PDUS scores for all joints examined.

Among the 81 patients with a DAS28-CRP ≤ 3.2 , 22 patients had synovial hyperemia detected on at least one joint (Power Doppler grade 1 in 13 patients, grade 2 in 6 patients and grade 3 in 3 patients). Patients with synovial hyperemia on at least one joint were more likely to have significantly increased levels of PIGF (18.9 ± 11.2 pg/mL vs. 13.1 ± 9.5 pg/mL, $p=0.022$) and Tie-2 (15.7 ± 5.8 ng/mL vs. 12.6 ± 3.4 ng/mL, $p=0.004$) than patients with absence of synovial hyperemia.

Conclusions: Serum levels of the angiogenic markers Tie-2, sVCAM-1 and Angiostatin were strongly associated with synovial vascularisation and inflammation assessed by PDUS among patients with established RA. Moreover, Tie-2 and PIGF were associated with persistent disease activity in RA patients in mow disease activity. These findings suggest that it may possible to find surrogate serum angiogenic biomarkers of active synovitis that might replace PDUS examination, in case of further confirmation of their pertinence.

Disclosure of Interest: A. Leblond: None declared, S. Pezet: None declared, A. P. Trouvin: None declared, M. Elhai: None declared, V. Gonzalez: None declared, Y. Allano: Grant/research support from: Pfizer, J. Avouac: None declared
DOI: 10.1136/annrheumdis-2018-eular.2709

THU0114 INFLUENCE OF AUTOANTIBODY STATUS IN TIME TO INITIATE DMARDS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

J. Molina Collada, M.G. González Álvarez, V. Navarro-Compán, L. Nuño Nuño, D. Peiteado, A. Villalba, P. Bogas, A. Balsa. *Rheumatology, Hospital La Paz, Madrid, Spain*

Background: Factors contributing to an early referral to Rheumatologist and DMARDs initiation following symptom onset in rheumatoid arthritis (RA) patients are unclear. Recent data suggest that ACPA/RF double seropositivity is associated with delayed presentation to primary care and DMARDs initiation. Identification of these factors is mandatory to facilitate an early diagnosis and treatment of RA patients.

Objectives: To determine whether time to DMARDs initiation and time to first visit at early arthritis clinic (EAC) following symptoms onset differs between RA patients according to autoantibody status.

Methods: A prospective analysis of an EAC cohort including 1377 referred patients from 1993 to 2017 was undertaken for this study. Patients diagnosed of RA (according to physician's diagnosis) were selected. Based on the serological status, we classified patients in 4 groups: RF+/ACPA+, RF-/ACPA+, RF+/ACPA-, RF-/ACPA-. A baseline clinical assessment was completed including time (months) from symptoms onset to first assessment at EAC and to DMARD initiation. First, differences between serotypes were tested using chi-squared and student-t tests. Second, univariable and multivariable logistic regression models taking into account confounding factors (age, smoking and baseline DAS28) were employed to evaluate the association between autoantibody status and both periods: time to first visit at EAC and to DMARDs initiation.

Results: A total of 463 RA patients were included for analysis, of whom 292 (63.1%) were RF/ACPA double-seropositive (RF+/ACPA+), 35 (7.6%) RF-/ACPA+, 39 (8.4%) RF+/ACPA- and 92 (19.9%) RF-/ACPA-. Demographic and clinical data are shown in table 1. In the univariate analysis, statistically significant differences were observed for both periods when patients were stratified by autoantibody serotype, where RF+/ACPA+ individuals experienced the longer delay to presentation at EAC compared with RF-/ACPA- (5.0 ± 4.6 vs 3.5 ± 3.4 months; $p<0.05$). RF+/ACPA+ patients experienced also significantly longer symptom duration before DMARD initiation than RF-/ACPA- (7.4 ± 1.2 vs 4.9 ± 5 months; $p<0.05$). In the univariable analysis, autoantibody status (double seropositive and RF-/ACPA+ vs RF-/ACPA-) was significantly associated with time to DMARDs initiation. However, after adjusting by confounding factors in the multivariable analysis, the autoantibody status did not remain significantly associated with time to initiate DMARDs (RF+/ACPA-; β 0.186; $p=0.1$, RF-/ACPA+; β 0.112; $p=0.3$, RF+/ACPA+; β 0.228; $p=0.1$)

	Beta	95% C.I.	
		Lower	Upper
Non adjusted			
RFpositive	,035	−2,462	4944
ACPApositive	,104	,038	7736
Double-seropositive	,120	,157	4791
Adjusted			
RF positive	,186	−4,952	26 414
ACPA positive	,112	−14,512	37 175
Double-seropositive	,228	−2,520	20 308
DAS 28	-,239	−7,575	,144
Age	-,073	-,384	,207
Smoker	-,066	−14,996	9118
Former smoker	-,081	−19,051	10 942

Abstract THU0114 – Table 1. Baseline characteristics of patients, stratified by autoantibody status

	Total n=463	RF+/ACPA+ n=292	RF-/ACPA+ n=35	RF+/ACPA- n=39	RF-/ACPA- n=92	p
Age	54.6 $\pm$ 16.3	54.0 $\pm$ 16.2	47.4 $\pm$ 16	60.2 $\pm$ 15.62	61.7 $\pm$ 16.8	<0.08
Sex	124 (26.1%)	70 (22.7%)	5 (13.3%)	14 (31.8%)	26 (24.3%)	NS
Race	364 (71.2%)	198 (64.3%)	31 (83.8%)	34 (77.3%)	91 (83%)	<0.001
Smoking	118 (23.1%)	74 (24%)	7 (18.9%)	12 (27.3%)	18 (16.8%)	<0.001
Smoker	109 (21.3%)	81 (26.9%)	9 (24.3%)	7 (15.9%)	8 (7.5%)	
Non smoker	236 (50.1%)	142 (46.1%)	17 (45.9%)	24 (54.5%)	73 (68.2%)	
Symmetry	60 (11.7%)	5 (1.4%)	8 (21.6%)	3 (6.8%)	2 (1.9%)	<0.01
Symmetric	44 (8.6%)	257 (83.4%)	29 (78.4%)	41 (93.2%)	101 (96.3%)	
Extension	89 (15.7%)	6 (1.4%)	1 (2.7%)	2 (4.5%)	1 (0.9%)	0.3
Monosarticular	3 (0.6%)	2 (0.6%)	1 (2.7%)	0 (0.0%)	0 (0.0%)	
Oligosarticular	3 (0.6%)	2 (0.6%)	1 (2.7%)	0 (0.0%)	0 (0.0%)	
Polysarticular	409 (80%)	238 (77.3%)	28 (75.7%)	38 (86.4%)	93 (86.9%)	
Polysarticular	1 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	
Time (months) from symptoms onset to DMARD initiation	6.9 $\pm$ 9.8	7.4 $\pm$ 11.2	8.8 $\pm$ 9.96	6.2 $\pm$ 7.2	4.9 $\pm$ 5	0.035
Time (months) from presentation at EAC to DMARD initiation	2.0 $\pm$ 1.1	2.2 $\pm$ 1.0.4	2.7 $\pm$ 1.0.3	2.0 $\pm$ 1.0	1.0 $\pm$ 1.8	0.7
Time (months) from symptoms onset to presentation at EAC	4.7 $\pm$ 4.4	5.0 $\pm$ 4.6	6.6 $\pm$ 4.9	4.2 $\pm$ 3.7	3.5 $\pm$ 3.4	0.019
Patient Global Assessment (0-100)	51.4 $\pm$ 26.2	50.9 $\pm$ 26.1	51.4 $\pm$ 26.9	51.2 $\pm$ 27.8	54.9 $\pm$ 25.3	NS
Physician Global Assessment (0-100)	37.6 $\pm$ 23.8	38.5 $\pm$ 23.3	34.2 $\pm$ 24.7	35.6 $\pm$ 25.3	38.6 $\pm$ 24.4	NS
HAQ	9.6 $\pm$ 6.3	9.2 $\pm$ 6.3	7.9 $\pm$ 4.2	10.3 $\pm$ 6.4	11.3 $\pm$ 6.1	<0.005
28 Tender Joint Count	8.5 $\pm$ 4.5	8 $\pm$ 4.2	6.1 $\pm$ 3.7	10.7 $\pm$ 5.7	9.9 $\pm$ 6.7	<0.001
28 Swollen Joint Count	6.7 $\pm$ 5.4	6.1 $\pm$ 5.1	4.3 $\pm$ 8	9.2 $\pm$ 6.2	9.5 $\pm$ 6	<0.001
DAS 28	5.2 $\pm$ 1.4	5.2 $\pm$ 1.42	4.5 $\pm$ 1.3	5.7 $\pm$ 1.3	5.6 $\pm$ 1.3	<0.001
ESR (mm/h)	36.1 $\pm$ 25.5	37.5 $\pm$ 26.1	25.6 $\pm$ 21	40.3 $\pm$ 23.2	35 $\pm$ 26.2	0.006

Conclusions: In our EAC cohort, time to EAC presentation and DMARD initiation following symptom onset in early RA does not differ according to patients' autoantibody status. However, more studies with greater sample size are necessary to confirm these results.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.5269

THU0115 PSYCHOLOGICAL AND FUNCTIONAL STATES PREDICT DISEASE FLARE FOLLOWING TNF INHIBITOR TAPERING IN PATIENTS WITH RHEUMATOID ARTHRITIS: A POST-HOC ANALYSIS OF DATA FROM THE OPTIMISING TNF TAPERING IN RA (OPTTIRA) COHORT

K. Bechman, F.E. Sin, F. Ibrahim, S. Norton, D. Scott, A. Cope, J. Galloway. *Rheumatology, King's College London, London, UK*

Background: Tapering or discontinuation of anti-TNF therapy appears to be feasible, safe and effective in a selected proportion of Rheumatoid Arthritis (RA) patients. Depression is highly prevalent in RA and may impact on flare incidence through a number of mechanisms. It is an independent predictor for flare in patients with active disease and is negatively associated with remission.¹ To date, there are no studies directly addressing the role of depression, anxiety or low mood in predicting flares in patients tapering their biological therapy.

Objectives: To investigate if psychological and functional states predict flare in RA patients with low disease activity (LDA) or in remission who undergo treatment tapering of their anti-TNF agents.

Methods: This study is a post-hoc analysis of the OPTTIRA trial,² a multi-centre, prospective, randomised, open label study investigating anti-TNF tapering in established RA patients in sustained LDA. Baseline patient-reported outcomes including HAQ-DI, EQ-5D, FACIT-F, and SF-36 including the Mental Health Index (MHI) component were collected. The MHI has been validated as a screening tool for depression in RA patients.³ The primary outcome was flare, defined as an increase in DAS28 ≥ 0.6 , and at least one additional swollen joint. Logistic regression was used to identify patient-reported outcomes that predict flare, adjusting for baseline covariates (age, gender, treatment arm, DAS28 and BMI).

Results: 97 were randomised into a tapering arm, either by 33% or 66% of their anti-TNF dose. The majority of patients were on methotrexate in combination with their anti-TNF therapy ($n=67$, 69%) and the median disease duration was 11 years [IQR: 7–17]. Seventy three (75%) fulfilled DAS28 remission criteria (DAS28 < 2.6). The median SF36 MHI score was 84. A score of ≤ 56 , the cut off used to detect depression was observed in 11% of patients. Forty one patients (42%) flared. Baseline DAS28 score was associated with flare, remaining significant after

adjusting for covariates [HR 1.96 (95% CI: 1.18, 3.24) $p=0.01$]. Disability (SF-36 physical component), fatigue (FACIT-F) and mental health (SF-36 MHI) predicted flare in univariate models (figure 1). In multivariate analyses, only MHI score remained a statistically significant independent predictor of flare [HR per 10 units 0.74 (95% CI: 0.60, 0.93) $p=0.01$].

Conclusions: Baseline DAS28 and mental health predict flare events in patients in LDA who taper their anti-TNF agents. Other psychological and functional states, measured by patient-reported outcome do predict flare events although the effect size is small and does not persist when adjusting for known predictors. Based on these findings, an assessment of functional and mental health states should be considered prior to biologic tapering.

REFERENCES:

- [1] Michelsen B, et al. Ann Rheum Dis 2017;76(11):1906–1910.
- [2] Ibrahim F, et al. Rheumatology 2017;56(11):2004–2014.

Acknowledgements : *Funding:* The trial was funded by Arthritis Research UK (grant reference number 18813)

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3077

THU0116 LIPID PROFILE AND CARDIOVASCULAR RISK IN SUBJECTS AT RISK FOR DEVELOPING RHEUMATOID ARTHRITIS

L. van Boheemen, M. van Beers - Tas, D. van Schaardenburg, M.T. Nurmohamed. *Rheumatology, Reade, Amsterdam, Netherlands*

Background: Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disease associated with an increased cardiovascular (CV) risk that is already present at the time of diagnosis. However, it is unclear at what point in the period before diagnosis of RA the CV risk increases. Therefore, we assessed the 10 year risk of CV morbidity and mortality in a cohort of subjects at risk for RA and analysed associations with anti-citrullinated protein antibody (ACPA) status and arthritis development.

Methods: In a cohort of 594 consecutive arthralgia patients with positivity for rheumatoid factor (RF) and/or ACPA, demographics, medical history, medication use and comorbidities were assessed. Lipid profile was determined and blood pressure was measured in a subset of patients. The 10 year CV risk score according to the Dutch CV risk management guideline (Dutch Systematic Coronary Risk Evaluations (SCORE)) was calculated for patients of whom data were complete.

Results: ACPA positive subjects ($n=382$) were younger (mean age 48.6 vs 51.6, $p=0.003$), more often smokers (31.8% vs 23.9%, $p=0.045$) and had lower cholesterol (mean level 5.2 vs 5.5, $p=0.001$) and HDL (mean level 1.1 vs 1.2, $p=0.004$) than ACPA negative subjects. Subjects who developed arthritis ($n=205$) had lower cholesterol (mean level 5.2 vs 5.4, $p=0.008$) and HDL levels (mean level 1.0 vs 1.2, $p=0.001$) and a higher TC/HDL ratio (median ratio 5.2 vs 4.8, $p=0.047$) compared to subjects who did not develop arthritis. Lower cholesterol (OR 1.24, CI 1.04–1.48), lower HDL (OR 2.01, CI 1.29–3.13) and higher TC/HDL ratio (OR 1.07, CI 1.00–1.138) predicted arthritis development.

The Dutch SCORE was calculated in 177 subjects (median 2, IQR 1–9). 76.4% had a low risk (SCORE <10%), 12.5% a medium risk (SCORE 10–<20%) and 11.4% had a high 10 year risk (SCORE >20%) of cardiovascular morbidity and mortality. The score was not associated with ACPA status or arthritis development.

Conclusions: Dyslipidemia as known in RA patients with active disease was also present in seropositive arthralgia patients at risk for RA, and predicted development of RA. However, arthralgia subjects who developed arthritis did not have a higher CV risk score than those who did not develop arthritis. Also, despite differences in lipid profile and smoking, the CV risk score does not differ between ACPA positive and ACPA negative subjects at risk for RA. Overall, differences in lipid profile predict development of RA but were too small to have an effect on the 10 year risk of CV morbidity and mortality as calculated by the Dutch CV risk score.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3936

THU0117 CHEMOKINE CCL18 ENRICHED IN SYNOVIAL FLUID IS INVOLVED IN JOINT DESTRUCTION THROUGH PROMOTING MIGRATION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS

Y.-Q. Mo¹, G.-C. Zhang², J. Jing¹, J.-D. Ma¹, L. Dai¹. ¹Rheumatology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University; ²Zhongshan School of Medicine, Sun Yat-Sen University, Guangzhou, China

Background: CC chemokine ligand 18 (CCL18) which is either constitutively expressed or induced in monocytes/macrophages and dendritic cells has been reported to be highly expressed in peripheral blood and synovial fluid of rheumatoid arthritis (RA) patients compared with healthy controls, indicating the possible role of CCL18 in the development and pathogenesis of RA.

Objectives: To explore the association of serum and synovial fluid CCL18 with clinical and radiographic outcome in RA patients and its potential effect on RA fibroblast-like synoviocytes (FLS).

Methods: Consecutive patients with active RA (DAS28-CRP>2.6) were recruited. Synovial fluid was collected from inflamed joints if available. Demographic and clinical data were collected according to the 2017 EULAR recommendation. Serum and synovial fluid CCL18 was detected by ELISA. RA-FLS was cultured *in vitro* with RA synovial fluid and neutralising antibody to CCL18. Migration/invasion ability was analysed by Transwell assay.

Results: (1) Among 83 RA patients, age (median and IQR, similarly hereinafter) was 50 (41–58) years old and 65 patients (78%) were female, with median disease duration 36 (12–102) months, median DAS28-CRP 5.0 (4.6–6.1). (2) Serum CCL18 was 107 (80–126) ng/mL, which was significantly higher than healthy controls [$n=25$, 51 (29–70) ng/mL, $p<0.001$, figure 1A]. Serum CCL18 correlated slightly but significantly with CRP ($r=0.385$, $p<0.001$), ESR ($r=0.239$, $p=0.03$), PrGA ($r=0.249$, $p=0.03$), DAS28-CRP ($r=0.368$, $p=0.001$), DAS28-ESR ($r=0.336$, $p=0.003$), SDAI ($r=0.360$, $p=0.001$), CDAI ($r=0.328$, $p=0.004$) and HAQ ($r=0.325$, $p=0.004$). (3) Synovial fluid CCL18 of 31 patients was 719 (415–1271) ng/mL, which was significantly higher than corresponding serum level (Paired test, $p<0.001$, figure 1A). Among them, 13 patients who were treated according to treat to target strategy received X-ray assessment of hand/wrist both at baseline and month 12. Six patients who had one-year radiographic progression (a change of the Sharp/van der Heijde modified sharp score ≥ 0.5 units) showed higher synovial fluid CCL18 than other 7 patients without radiographic progression [1481 (1244–2034) ng/mL vs. 458 (405–681) ng/mL, $p=0.004$, figure 1B). (4) When incubated with RA synovial fluid, the migration ability of RA-FLS was significantly increased; but this effect was inhibited by neutralising antibody to CCL18 (figure 1C).

Abstract THU0117 – Figure 1. Chemokine CCL18 which was enriched in RA synovial fluid promoted migration of fibroblast-like synoviocytes in Rheumatoid Arthritis (RA), but was inhibited by neutralising antibody to CCL18. A: Comparison of RA synovial fluid CCL18 with serum CCL18 of RA patients and health controls. B: Comparison of RA synovial fluid CCL18 between patients with and without one-year radiographic progression. C: Transwell assay, crystal violet staining for RA-FLS (purple), with original magnification of $\times 100$.

** $p<0.001$, *** $p<0.0001$