Methods: A Nordic (Denmark, Finland, Norway, Sweden) open-label, single-arm study (part of the umbrella program – TOZURA (1)), enrolled patients with inadequate response to conventional synthetic (cs) DMARDs. Patients received tocilizumab 162mg sc weekly for 24 weeks as monotherapy or in combination with a csDMARD. Stable oral NSAIDs and corticosteroids (≤ 10 mg/day prednisone or equivalent), were allowed. Patients were assessed at baseline, 4, 12 and 24 weeks for fatigue (FACIT-F questionnaire (total sum scores)), patient reported outcome measures (PROMs) including joint pain and patient's global visual analogue scale (VAS) as well as HAQ-DI, clinical assessments (tender and swollen joints, assessor's global VAS), laboratory examinations (ESR, CRP) and ultrasound assessments (36 joints and 4 tendons, scored according to the Norwegian US atlas (2)). Spearman correlations, performed both at baseline and for changes from baseline of variables during follow-up, explored associations between fatigue and PROMs, clinical, laboratory as well as ultrasound variables. Predictive value of fatigue was investigated by linear regression.

Results: 110 patients were included (83% female, mean (SD) age 55.6 (12.1) years and RA duration 8.7 (9.5) years, 81% anti-CCP positive). All PROMs, clinical, laboratory and ultrasound variables decreased significantly, already after 4 weeks ($p < 0.001$). Both for baseline assessments as well as for changes during follow-up, fatigue was associated with PROMs (Table 1 (baseline) and Table 2 (follow-up)). However, there were no or low associations between fatigue and clinical, laboratory and ultrasound assessments at baseline or during follow-up. In addition, baseline fatigue was predictive of joint pain, patient's global VAS and HAQ-DI during follow-up ($p < 0.05$ – 0.001), but not for the clinical, laboratory or ultrasound assessments.

Conclusion: Fatigue assessed by an established questionnaire did not show any associations with several assessments of inflammatory activity in RA patients, neither at baseline nor during effective treatment. Thus, the present study adds to the increasing number of papers finding fatigue to reflect other aspects of RA disease activity than inflammation.

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Table 1. Spearman correlations between FACIT-F total score and patient reported outcomes, clinical, laboratory and ultrasound assessments. * $p < 0.05$. ** $p < 0.001$

	Baseline	4 weeks	12 weeks	24 weeks
Patient's global VAS	-0.46**	-0.41**	-0.50**	-0.48**
Joint pain VAS	-0.43**	-0.50**	-0.54**	-0.41**
HAQ-DI	-0.59**	-0.59**	-0.60**	-0.62**
28 tender joint count	-0.07	-0.19	-0.12	-0.22*
28 swollen joint count	0.14	0.12	0.20*	0.19
Examiner's global VAS	0.05	0.05	-0.03	-0.15
ESR (mm/h)	-0.02	-0.01	0.07	-0.04
CRP (mg/L)	-0.11	-0.02	0.06	0.07
Sum score GS	0.09	0.20*	0.24*	0.13
Sum score Doppler	0.06	0.01	0.13	0.02

Table 2. Spearman correlations between changes in FACIT-F total score from baseline to 4, 12 and 24 weeks and changes in patient reported outcomes, clinical, laboratory and ultrasound assessments. * $p < 0.05$. ** $p < 0.001$

	4 weeks	12 weeks	24 weeks
Patient's global VAS	-0.59**	-0.56**	-0.59**
Joint pain VAS	-0.60**	-0.50**	-0.52**
HAQ-DI	-0.43**	-0.44**	-0.61**
28 tender joint count	-0.29*	-0.30*	-0.24*
28 swollen joint count	-0.15	-0.17	-0.06
Examiner's global VAS	-0.14	-0.27*	-0.15
CRP (mg/L)	-0.19	-0.21*	-0.25*
ESR (mm/h)	-0.13	-0.18	-0.21
Sum score GS	-0.10	-0.17	-0.12
Sum score Doppler	-0.21*	-0.14	-0.10

Disclosure of Interests: Hilde Berner Hammer Speakers bureau: AbbVie, Pfizer, Roche, Lilly and Novartis, Consultant of: Novartis, Birté Aguilar Employee

of: Roche, Lene Terslev Speakers bureau: Roche, MSD, BMS, Pfizer, AbbVie, Novartis and Janssen

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POS0308 TRAJECTORIES OF FATIGUE IN EARLY RA OVER 10 YEARS: RESULTS FROM THE ESPOIR COHORT

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Background: Fatigue is one of the most prevalent symptom reported by persons with RA. RA-related fatigue is a complex concept with biological, psychological and social interactions.

Objectives: In a cohort of early RA patients, to determine and characterize fatigue trajectories over 10 years of follow-up and identify predictors of trajectory membership.

Methods: Patients fulfilling the 2010 ACR/EULAR criteria for RA included in the ESPOIR cohort. We used a cluster analysis to obtain fatigue (assessed by fatigue visual analogue scale) trajectories over the course of 10 years from enrolment. Chi-square tests or ANOVA were performed to evaluate differences of baseline variables between fatigue trajectories. Using a multinomial logistic regression we could identify predictors of trajectory membership.

Results: We analysed 598 patients with mean disease duration at enrolment of 26.2 ± 40.9 days. Cluster analysis revealed 3 trajectories: high (18%), moderate (52%) and low fatigue (30%). Compared to patients with moderate or low fatigue trajectory, patients with high fatigue trajectory were predominantly women and reported significantly higher duration and intensity of morning stiffness, HAQ score, number of tender joints, levels of pain, number of awakenings due to arthritis, levels of physician and patient global assessment and more frequent sleep problems, and increased psychological distress. Female patients with pain, psychological distress and presence of sicca symptoms had higher risk of being in high trajectory group.

Conclusion: These findings suggest that levels of fatigue are rather stable over time in each trajectory. Baseline clinical measures and baseline patient-reported measures of functional status better distinguished the three fatigue trajectories. We did not find differences between trajectories in baseline laboratory measures. Inflammatory activity was not a predictor of being in high trajectory fatigue group.

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POS0309 SEROPOSITIVITY INCREASES RISK OF INCIDENT DEMENTIA IN INDIVIDUALS WITH RHEUMATOID ARTHRITIS: A POPULATION-BASED COHORT STUDY

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Background: Several studies show increased risk of dementia among individuals with rheumatoid arthritis (RA), while others show no association. One reason for this discrepancy might be differential association by serostatus. No prior studies have investigated the association between RA and dementia by serostatus.

Objectives: We aimed to evaluate the risk of incident dementia among individuals with RA, stratified by serostatus.

Methods: This population-based cohort study included all cases of incident RA within Olmsted County, Minnesota with index date of RA onset between 1 January 1999 and 31 December 2013. We matched RA cases to non-RA comparators 1:1 on age and sex. All RA cases met 1987 ACR criteria for RA. We defined seropositivity as positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies. We defined incident dementia as having two ICD-9/10 codes for dementia at least 30 days apart, with the date of the second code representing the time of dementia onset. We excluded individuals with dementia prior to index date. We estimated the cumulative incidence of dementia adjusting for the competing risk of death. For the main analysis, cox proportional hazard models estimated adjusted hazard ratios (aHR) with 95% confidence intervals (CI) for incident dementia, adjusting for age, sex, index year, body mass index, and smoking status (never, former, current). These models compared the incidence of dementia for RA versus non-RA, seropositive and seronegative RA versus their matches, and seropositive versus seronegative RA. To validate these results, we also performed sensitivity analyses using groups matched via inverse probability weighting on age, sex, index year, obesity, smoking status, and race.

Results: We identified 597 RA cases (mean age 56, 70% female), and 594 non-RA comparators. Of the RA cases, 388 (65%) were seropositive, and 209 (35%) were seronegative. The ten-year cumulative incidence of dementia in patients with RA was 3.3 (95%CI 2.0,5.5) per 100,000 compared to 2.4 (95%CI 1.3,4.2) in non-RA comparators, for aHR of 1.26 (95%CI 0.7,2.3). When stratifying by serostatus, the ten-year incidence of dementia for seropositive RA cases was 3.6 (95%CI 2.0,6.5), corresponding to aHR of 1.45 (95%CI 0.73,2.9) compared to matched non-RA cases. In contrast, the incidence of dementia in seronegative RA cases was 2.6 (95%CI 1.0,7.0), for an aHR of 1.0 (95%CI 0.29,3.5). Overall, the incidence of dementia in seropositive RA cases was significantly higher than seronegative cases (aHR 3.2, 95%CI 1.2,8.5). Indeed, sensitivity analysis using inverse probability weighting confirmed that among participants aged 50 and older, dementia incidence was higher for seropositive than seronegative RA (aHR 2.9, 95%CI 1.1,7.8) (Figure 1).

Conclusion: Individuals with seropositive RA have an increased risk for incident dementia than those with seronegative RA. Future studies should replicate these findings and investigate the mechanism for this association.

Figure 1. Cumulative incidence of dementia for individuals with seropositive versus seronegative RA aged 50 and older, balanced by inverse probability weighting

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POS0310

EXPOSURE TO MAJOR PSYCHOLOGICAL TRAUMA OR STRESS IN THE PRECEDING ONE YEAR SIGNIFICANTLY CONTRIBUTES TO POOR DISEASE CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS: SINGLE CENTRE RESULTS FROM THE PRIME REGISTRY COHORT

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Background: Stress response is considered to involve the activation of both the hypothalamus-pituitary-adrenal axis and the autonomic nervous system, along with its communication with the immune system. Because many rheumatic diseases are characterized by immune-mediated joint inflammation, stressful events might contribute to the aetiology, maintenance and exacerbation of rheumatic diseases.

Objectives: We aimed to examine whether real-life major stressful events lead to poor disease control among patients with Rheumatoid arthritis (RA). We addressed this question using real-world data from the PRIME registry.

Methods: This was a cross-sectional study conducted using data collected at the time of patient enrolment in the PRIME registry. The PRIME Registry is a large, independent, prospective, observational cohort initiated in October 2019 that comprises patients diagnosed with RA, SLE, PsA or AS by a rheumatologist, and is being actively followed up. IRB approval and informed consent was obtained. We assessed the registry data for RA patients. The clinical variables studied were gender, age, smoking habits, body mass index, education status, marital status, disease duration, comorbidities (using Charlson Comorbidity Index). Education status was stratified by whether participants completed secondary (high) school education. Evaluation of disease activity and severity was made as per internationally agreed definitions, such as: swollen joint counts (SJC), tender joint counts (TJC), deformed joint counts, and DAS-28. Major psychological trauma or stress was defined if the patient has experienced any of the following in the past year: a) major personal injury or illness; b) death/major illness of a close relative; c) marital separation/divorce; d) loss of job; e) major financial loss; f) mass casualty incident loss.

Results: The data of consecutive 507 RA patients (mean age 42.3±12.6 years, 73.6% female, disease duration of 80±22 months) was reviewed. Thirty-six percent of the cohort reported to have major psychological stress and trauma in the preceding one year. No statistical association of age, gender, and marital status was noted, but statistical association of low education status (p=0.042), longer disease duration (p=0.044), higher DAS-28 values (p<0.001) and other markers of RA disease activity (SJC, TJC, ESR, patient global health) was found. On multiple logistic regression analysis, a significant association of major psychological stress and trauma in the preceding one year was noted with active disease (DAS-28; OR 1.67, CI 1.17-2.4, p=0.005). Following variables were included in the full regression model, disease duration, gender, age, marital status, education status, and DAS-28 value (also used models with SJC, TJC, deformed joint counts, ESR, patient global health, but the results remained unchanged).

Conclusion: Major psychological stress and trauma in the preceding one year is associated with high disease activity among patients with RA. Therapies that focus on stress management may be important adjuncts to traditional pharmacotherapy in the treatment of inflammatory rheumatic diseases.

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POS0311

NEUROIMAGING BIOMARKERS IN INDIVIDUALS WITH AND WITHOUT RHEUMATOID ARTHRITIS: RESULTS FROM THE MAYO CLINIC STUDY OF AGING

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Background: Age-related increase in the burden of systemic inflammation is an established key player and potential treatment target in Alzheimer's disease (AD) and other age-related dementias. (Dregan, Chowienczyk et al. 2015) Although rheumatoid arthritis (RA) is an autoimmune hyper-inflammatory disease, studies on RA and dementia or vascular neuroimaging biomarkers are lacking.

Objectives: To examine the associations between RA and dementia/vascular neuroimaging biomarkers in the Mayo Clinic Study of Aging (MCSA).