Conclusion: In this small study, seropositivity and disease activity were higher in responders. Baseline immunohistochemical staining was not a good discriminator of treatment responses

Disclosure of Interests: Kieran Murray Grant/research support from: Bresnihan Molloy and Newman fellowships, Candice Low: None declared, Francis Young: None declared, Monika Bienicka: None declared, Elmeir Mylod: None declared, Ursula Fearon: None declared, Douglas Veale: None declared

DOI: 10.1136/annrheumdis-2021-eular.2593

POS0478

ASSOCIATION BETWEEN BODY SHAPES AND BODY SHAPE TRAJECTORIES, AND THE RISK OF RHEUMATOID ARTHRITIS IN THE FRENCH E3N COHORT

C. Salliot^{1,2,3}, Y. Nguyen^{4,5}, X. Mariette^{3,6}, M. C. Boutron-Ruault^{2,7}, R. Sero^{3,8}, ¹Centre Hospitalier d'Orleans, Rheumatology, Orleans, France; ²Center for Research in Epidemiology and Population Health (CESP), Université Paris-Saclay, Institut pour la Santé et la Recherche Médicale (INSERM) U1018, Villejuif, France; ³Center of Immunology of Viral Infections and Auto-immune Diseases (IMVA), Université Paris-Saclay, Institut pour la Santé et la Recherche Médicale (INSERM) U1184, Le Kremlin Bicêtre, France; ⁴Hôpital Beaujon, Université de Paris, Internal Medicine, Clichy, France; ⁵Center for Research in Epidemiology and Population Health (CESP), Paris-Saclay, Institut pour la Santé et la Recherche Médicale (INSERM) U1018, Villejuif, France; ⁶Assistance Publique-Hôpitaux de Paris (AP-HP), AP-HP Université Paris-Saclay – Hôpital Bicêtre, Rheumatology, Kremlin Bicêtre, France; ⁷Institut Gustave Roussy, Université Paris Saclay, Villejuif, France; ⁸Assistance Publique-Hôpitaux de Paris (AP-HP), AP-HP Université Paris-Saclay – Hôpital Bicêtre, Rheumatology, Le Kremlin Bicêtre, France

Background: Several cohort and case-control studies have suggested that overweight or obesity is associated with the risk of Rheumatoid Arthritis (RA). Associations were based on Body Mass Index (BMI), although this measurement does not reflect the fat distribution [1].

Objectives: To study the relationships between anthropometric measurements and the risk of RA in women involved in the E3N cohort.

Methods: E3N is an ongoing French prospective cohort that enrolled 98,995 women aged 40-65 years in 1990. Women completed mailed questionnaires every 2-3 years on lifestyle and health-related information. A total of 698 incident RA cases have been validated among 78,452 women [2]. Available anthropometric measurements include birth height and weight, height and weight (collected at baseline and regularly updated during follow-up), and age-related body shapes (BS). Women had to identify the silhouette among 8 BS that best described their BS at 8 years, puberty, 20-25 years, 30-35 years, and study baseline. BS trajectories (from 8 to 30-35 years) were constructed using Nagin's approach to group-based trajectory modeling that identifies 6 different trajectories [3]. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of incident RA were estimated using Cox proportional hazards regression models with age as the time scale. Models were first adjusted for known risk factors of RA (model 1), and then multi-adjusted (model 2).

Results: Taking lean BS as reference, medium BS at puberty was associated with an increased risk of RA [HR=1.23 (95% CI 1.0-1.5)], in the fully adjusted model (table 1), as was large BS at baseline [HR =1.32 (95% CI 1.1-1.6)] (in model 1). Obesity (BMI>30 kg/m²) was marginally associated with RA in model 1 [HR=1.30 (95% CI 1.0-1.7)], but the association was no longer statistically

Table 1. Cox proportional-hazards analysis of anthropometric factors associated with RA

RA	Non-cases	MODEL 1		MODEL 2		
		HRs (95%CI)	<i>ptrend</i>	HRs (95%CI)	<i>ptrend</i>	
Baseline Body mass index (kg/m ²)						
<18	10	1,797	0.75 (0.4-1.4)	0.0532	0.85 (0.4-1.6)	0.6165
[18-25]	462	50,330	Ref		Ref	
[25-30]	171	19,716	1.10 (0.9-1.3)		1.00 (0.8-1.2)	
> 30	55	5,911	1.30 (1.0-1.7)		1.13 (0.8-1.6)	
Body shape at puberty						
Lean	332	40,485	Ref	0.0937	Ref	0.1490
Medium	179	17,903	1.24 (1.0-1.5)		1.23 (1.0-1.5)	
Large	147	15,984	1.14 (0.9-1.4)		1.12 (0.9-1.4)	
Body shape at baseline						
Lean	359	44,718	Ref	0.0055	Ref	0.1743
Medium	200	20,041	1.20 (1.0-1.4)		1.16 (0.9-1.4)	
Large	110	9,838	1.32 (1.1-1.6)		1.20 (0.9-1.6)	

ptrend: p for trend. Ref: reference.

significant in the multi-adjusted model, taking normal BMI [18-25 kg/m²] as the reference.

Birth weight and height, BS (at 8, 20-25 and 30-35 years), and BS trajectories were not significantly associated with RA in any model.

Conclusion: In E3N cohort, medium body shape at puberty was associated with an increased risk of RA independently of the BMI and smoking exposure.

Model 1 adjusted for age, smoking (past/current/never), passive smoking during childhood and/or adulthood (ever/never), educational level (<high-school, up to 2 years of university, ≥ 3 years of university).

Multi-adjusted model 2 included model 1 + body mass index (<18, 18-25, 25-30, >30 kg/m²), body shape at puberty, body shape at baseline adjusted for age, baseline physical activity (in quartiles), age at menarche (<13, 13-15, ≥15 years), age at menopause (≤45, 45-53, ≥53 years), age at the first pregnancy (<22, 22-27, ≥27 years), number of full-term pregnancies (≤1, 2, ≥3), and duration of premenopausal use of progestogen (0, 0-24, >24 months).

REFERENCES:

- [1] Crowson CS, Matteson EL, Davis JM 3rd, Gabriel SE. Contribution of obesity to the rise in incidence of rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2013;65:71-7.
- [2] Nguyen Y, Salliot C, Gusto G, et al. Improving accuracy of self-reported diagnoses of rheumatoid arthritis in the French prospective E3N-EPIC cohort: a validation study. *BMJ Open*. 2019;9:e033536.
- [3] Nagin D. Analyzing developmental trajectories: a semiparametric, group based approach. *Psychol Methods* 1999;4:139e57.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2655

POS0479

THE IMPACT OF FLARES ON PATIENT REPORTED OUTCOMES IN RHEUMATOID AND UNDIFFERENTIATED ARTHRITIS PATIENTS – A SUB-ANALYSIS OF THE IMPROVED STUDY

J.M. Maassen¹, S.A. Bergstra¹, P.D. de Buck², M. van Oosterhout³, T. Huizinga¹, C. Allaart¹. ¹Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands; ²Haaglanden Medical Center, Rheumatology, The Hague, Netherlands; ³Groene Hart Hospital, Rheumatology, Gouda, Netherlands

Background: In rheumatoid arthritis (RA) patients in low disease activity, flares are associated with symptom deterioration. Patients in clinical remission may flare but still have low disease activity. How does this affect patient reported outcomes?

Objectives: To evaluate the prevalence of disease flares in patients treated to target drug free remission, and to study the impact of disease flares on patient-reported outcomes (PROs) for flares with different impact on disease activity.

Methods: In the IMPROVED study 610 patients with rheumatoid arthritis (RA) or undifferentiated arthritis (UA) were treated to target drug free remission (DAS <1.6) for 5 years. As soon as DAS was ≥1.6, treatment was tapered to discontinuation. Patients with at least 8 months follow-up were selected. A flare was defined according to three definitions; **A)** DAS ≥1.6 and ≥0.6 increase from the previous visit regardless of the previous DAS; **B)** minor flare from remission; a DAS ≥1.6 with <0.6 increase and previous DAS <1.6; **C)** major flare from remission; a DAS ≥1.6 with ≥0.6 increase and previous DAS <1.6. Linear mixed models were used to compare functional ability, measured by the health assessment questionnaire (HAQ), at visits where a flare occurred versus visits without a flare. Fisher's exact test were used to compare percentages with ≥0.22 HAQ increases between groups with and without LDA at the moment of flare. A generalized linear mixed model was used to calculate the odds ratio for a deterioration of ≥20mm in VAS of PROs global health (GH), disease activity, pain and morning stiffness (from the preceding visit) during a flare.

Results: Of the 585 patients with sufficient follow-up, 75% experienced a flare **A**, 26% a flare **B**, and 68% a flare **C**, at least once. Most flares were observed after t=8 and t=12 months. In 55%, 100%, and 69% of visits with a flare A, B or C, the patients were still in LDA (DAS=<2.4). In 55% of the visits where a flare was associated with a DAS increase ≥0.6 (flare A & C) there was also clinically relevant increase in HAQ of ≥0.22. The mean difference in HAQ was 0.27 with flare **A** (p<0.01), 0.03 with flare **B** (p=0.72) and 0.18 with flare **C** (p<0.01). If was DAS >2.4 (LDA) at the moment of flare, HAQ increased ≥0.22 in 68% of all flares A, and 77% of all flares C (p-values <0.01, compared to flares where patients were still in LDA, DAS=<2.4). The odds ratios of a >20mm deterioration in VAS global health, VAS disease activity, VAS pain and VAS morning stiffness was significant ≥1 for flares with a ≥0.6 increase in DAS (flares A and C), and ≤1 for minor flares (B) (table 1).

Conclusion: In early arthritis patients, during 5 years treated to target drug free DAS-remission, disease flares with loss of DAS-remission were common. Although the majority of patients who flared were still in LDA, most reported more pain, morning stiffness, increased disease activity and a diminished global health. On average, deterioration in HAQ only exceeded the minimum clinically important difference (delta HAQ ≥ 0.22) in case of a ≥ 0.6 increase in DAS, independent of the previous DAS. Depending on the definition of flare, up to 45% of patients lost DAS LDA, and in this group the functional deterioration significantly more often exceeded the MCID as compared to the patients that flared but were still in LDA. More research is needed to find out which patients are most at risk for clinically relevant flares, and to evaluate the impact of flares in patients with remission on long term outcomes.

Table 1. Odds Ratios and 95% confidence intervals for > 20mm increase in PROs on 100mm visual analogue scales

	Flare A		Flare B (minor)		Flare C (major)	
	Prevalence ≥ 20 mm ^a	OR (95% CI)	Prevalence ≥ 20 mm ^a	OR (95% CI)	Prevalence ≥ 20 mm ^a	OR (95% CI)
Global health	62%	2.1 (1.5; 2.8)	45%	0.5 (0.4; 0.7)	62%	1.4 (1.1; 1.8)
Disease activity	62%	2.5 (1.7; 3.8)	45%	0.4 (0.3; 0.6)	62%	2.1 (1.4; 3.0)
Pain	87%	2.0 (1.3; 3.1)	78%	0.5 (0.3; 0.8)	87%	1.8 (1.2; 2.5)
Morning stiffness	84%	1.7 (1.1; 2.6)	77%	0.6 (0.4; 0.9)	86%	2.1 (1.5; 2.9)

^a The prevalence of ≥ 20 mm deterioration in VAS PRO's during a visit with a flare.

Acknowledgements: We would like to thank all patients for their contribution as well as the rheumatologists who participated in the IMPROVED-study group. We would also like to thank all other rheumatologists and trainee rheumatologists who enrolled patients in these studies, and all research nurses for their contributions.

Disclosure of Interests: Johanna M. Maassen: None declared, Sytske Anne Bergstra: None declared, Petronella DM de Buck: None declared, M. van Oosterhout: None declared, Thomas Huizinga: None declared, Cornelia Allaart Grant/research support from: the IMPROVED study was designed by the investigators and financially supported by AbbVie in the first year.

DOI: 10.1136/annrheumdis-2021-eular.2656

POS0480 ASSOCIATION OF NEUTROPHIL LYMPHOCYTE AND PLATELET LYMPHOCYTE RATIOS WITH JOINT INFLAMMATION IN RHEUMATOID ARTHRITIS

D. Pearce-Fisher^{1,2}, D. Orange^{1,2}, B. Mehta^{1,3}, D. Jannat-Khah^{1,3}, S. Goodman^{1,3}.

¹Hospital for Special Surgery, Medicine, New York, United States of America;

²The Rockefeller University, Clinical Investigation, New York, United States of America;

³Weill Cornell Medicine, Medicine, New York, United States of America

Background: Some patients with rheumatoid arthritis (RA) have high disease activity scores (DAS) and low synovial inflammation, and others have high synovial inflammation and low DAS (subclinical synovitis)[1]. It would be clinically useful to identify blood biomarkers of synovial inflammation. Neutrophil-lymphocyte (NLR) and platelet-lymphocyte ratios (PLR) have been reported to distinguish RA patients with moderate/high DAS28 scores from low DAS28 [2]. However, it is not known if these inexpensive, accessible tests are associated with inflammation in synovial tissue at the histological level.

Objectives: The objective of this study was to evaluate the relationship of pre-operative NLR and PLR with synovial inflammation of the operative joint in RA patients undergoing arthroplasty.

Methods: 230 patients meeting ACR/EULAR 1987 and/or 2010 criteria were recruited prior to elective total hip, knee, shoulder, and elbow replacement. Demographics, RA characteristics, medications, disease activity, and routine tests including complete blood tests (CBC) were collected pre-operatively. Hematoxylin and eosin (H&E) stains were prepared from the synovium of the operative joint and systematically scored by a pathologist as described previously [3]. Synovial lymphocytic inflammation was graded as none, mild, moderate, marked, or band-like. Linear regression was performed to distinguish differences in the NLR, PLR, and CRP in patients with synovial lymphocytic inflammation (SLI).

Results: As expected, patients on glucocorticoids (GCs) had higher NLR (mean 5.52 (SD 7.68) vs mean 2.82 (SD 1.66) ($p < 0.001$) and higher PLR (mean 233.73 (SD 237.21) vs (mean 162.93 (SD 65.35)) (p -value=0.04)) and those patients (N=92) were therefore excluded from down-stream analyses. On the remaining 138 patients, we tested for associations of PLR, NLR and CRP with SLI using linear regression. In all the models the highest category for synovial lymphocytic inflammation was found to be statistically significantly associated with NLR, PLR and CRP, separately (Table 1).

Table 1. Results from linear regressions evaluating the association of NLR, PLR, and CRP with synovial lymphocytic inflammation.

Linear regression Results	NLR	PLR	CRP
Synovial Lymphocytic Inflammation Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
None	Reference	reference	reference
Mild	0.31 (-0.51, 1.13)	26.54 (-8.83, 61.90)	-1.00 (-2.37, 0.36)
Moderate	0.73 (-0.18, 1.64)	28.66 (-10.22, 67.53)	0.46 (-1.09, 2.01)
Marked	0.21 (-0.80, 1.22)	24.62 (-22.80, 72.05)	0.81 (-0.87, 2.49)
Band-like	1.92 (0.81, 3.02)	80.42 (31.46, 129.38)	2.32 (0.49, 4.16)

OR= Odds ratio, Coef = Coefficient, NLR= neutrophil lymphocyte, PLR= platelet lymphocyte ratio, CRP= C-reactive protein All significant associations are bolded.

Conclusion: NLR, PLR and CRP are associated with high synovial lymphocytic inflammation of the operative joint. This suggests that these inexpensive, routinely performed blood tests may be a useful blood biomarker of synovial inflammation.

REFERENCES:

- [1] Orange, D.E. *et al.* Histologic and Transcriptional Evidence of Subclinical Synovial Inflammation in Patients With Rheumatoid Arthritis in Clinical Remission. *Arthritis Rheumatol.* 71(7): 1034-1041 (2019).
- [2] Lee, Y.H. Association between the Neutrophil-to-lymphocyte Ratio, and Platelet-to-lymphocyte Ratio and Rheumatoid Arthritis and their Correlations with the Disease Activity: A Meta-analysis. *J Rheum Dis.* 25(3):169-178 (2018).
- [3] Orange, D. E. *et al.* Identification of Three Rheumatoid Arthritis Disease Subtypes by Machine Learning Integration of Synovial Histologic Features and RNA Sequencing Data. *Arthritis Rheumatol. Hoboken NJ* 70: 690-701 (2018).

Disclosure of Interests: Diyu Pearce-Fisher: None declared, Dana Orange Consultant of: Astra Zeneca/MedImmune and Pfizer, Bella Mehta Consultant of: Novartis, Deanna Jannat-Khah: None declared, Susan Goodman Consultant of: UCB, Grant/research support from: Novartis, Horizon Pharmaceuticals

DOI: 10.1136/annrheumdis-2021-eular.2729

POS0481 DOES OLDER REALLY MEAN WISER?

D. Khalifa¹, S. Belghali¹, M. Limam², N. El Amri¹, K. Baccouche¹, H. Zeglaoui¹, E. Bouajina¹. ¹Farhat Hached Hospital, Rheumatology, Sousse, Tunisia; ²Farhat Hached Hospital, Preventive Medicine, Sousse, Tunisia

Background: One of the main challenges in Rheumatoid arthritis (RA) is to maintain remission or low disease activity by adhering to the prescribed treatments. However, it is believed that adherence to long term treatments is inadequate in chronic diseases. Does this apply to older people too?

Objectives: To assess treatment adherence among an elderly RA population and to study determining factors of non-adherence

Methods: A cross-sectional study over a period of 4 months was conducted in a rheumatology clinic (September 2020-December 2020). Consenting elderly over the age of 65 presenting with RA were included. Exclusion criteria involved associated connective tissue diseases and troubles communicating. During clinical visits, sociodemographic information, clinical, radiological and therapeutic data were collected. Treatment adherence was assessed by the 5-item compliance questionnaire of rheumatology (CQR-5). Patients were also asked about the degree of satisfaction vis-à-vis the therapeutic effect detected. Univariate and multivariate analysis were conducted using the statistical tool SPSS.20.

Results: Forty patients consented to join the study, 82.5% of them were women. The median of age was 66.5 years old with a minimum of 65 and a maximum of 83. Comorbidities were noted in 55% of the patients. 75% of the patients had health insurance. The mean pain score was 5 out of 10 on a visual analog scale (VAS). The mean DAS 28 was 4.65 $\pm$ 1.77 with 72.5%