premature CHD. Classical risk factors are observed more frequently in CHD patients as expected but interestingly, no additional risk factors other than age were detected between premature and other CHD patients. This suggests that the primary factor triggers premature CHD is the underlying inflammatory rheumatic disease. The presence of CHD was determined by patient history which the limitation of our study. We did not assess to subclinical CHD in this study.

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THU0132 IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE FOR PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 2-YEAR FOLLOW UP

M.S. Sergeeva, B.S. Belov, G.M. Tarasova, E.N. Alexandrova, A.A. Novikov, M.V. Cherkasova, D.E. Karateev, E.L. Luchikhina, Y.V. Muravyev, D.V. Buhanova. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Comorbid infections have significant impact on morbidity and mortality, especially in autoimmune diseases. Prevention of infection is an integral part of supervision of these patients.
Objectives: To investigateimmunogenicity and safety of 23-valent polysaccharide pneumococcal vaccine in patients with rheumatoid arthritis (RA) treated with diseases modifying anti rheumatic drugs (DMARDs) and biologic diseases modifying anti rheumatic drugs (bDMARDs) during the 2-year follow-up.
Methods: Out of 110 subjects (81 females (73,6%), 29 males (26,4%) aged 23–76 years) included into the study, 79 were RA patients and 31 were controls with a history of ≥2 episodes of lower respiratory tract infections (bronchitis, pneumonia). 52 patients with RA were on methotrexate (MTX), 14 were on leflunomide (LEF), 13 were ontumor necrosis factor alpha inhibitors (iTNF-α)+MTX. One dose (0,5 ml) of 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously without discontinuation of MTX/LEF or 28–30 days prior to initiation of iTNF-α. Totally four study visits were preplanned: initial vaccination visit and 3 control visits in 1, 3 and 12 months after vaccinationfor 110 patients. 39 RA patients were followed up for 2 years (24 months). Routine evaluation during each visit included physical exams and laboratory tests. Levels of antibodies to pneumococcal capsular polysaccharide were measured using VaccZymeTM PCPIgG 2 kit (The Binding Site Group Ltd, Birmingham, UK). Post-immunization response coefficient was calculated for each participant as the ratio of AB levels during visits II, III, IV and V to baseline AB level at Visit I.
Results: Not a single caseof clinicallyor radiographically confirmed pneumonia was documented during the follow up period. Pronounced positive immune reaction after administration of the vaccine under investigation was documented in RA patients during different therapies, i.e., significant post-immunization response coefficient increase. There were 61% responders among RA patients and 70% responders among the controls during one-year follow-up. Dynamics of post-immunization response coefficient in RA patients during 2-year follow up are presented in the Table. RA patients and the control group are marked more than 2-foldsignificant increase in the content of antibodies in 3 monthsafter the vaccination. Despite the decline in their concentrationsto 12 months, it remained at the proper level and was increased to 24 month follow-up.Good tolerability of the vaccine was documented in 65% of cases, satisfactory (injection site pain, swelling and hyperemia of the skin up to 2 cm in diameter and subfebrilefever) in 35% of cases. As these reactions had no causal relationship with current RA therapy, and fully resolved within 24 hours without additional treatment, no RA therapy modification was required.Pronounced DAS28 positive dynamics in RA patients (4,27 and 2,68 at Visit I and Visit V, respectively, $p<0,001$) indicates the absence of any negative impact of vaccination on disease activity.

Table. Post-immunization response coefficient dynamics in RA patients during 2 year follow up, Me [25,75 percentile], (n=39).

	Visit II (1 month)	Visit III (3 Month)	Visit IV (12 month)	Visit V (24 month)
RA patients	2,33* [1,6;3,8]	3,55* [2,32;6,23]	2,64* [2,03;6,39]	3,07* [1,56;6,18]

*$p<0,05$

Conclusions: Thus, all given prove the sufficient immunogenicity and safety of 23-valent pneumococcal vaccine in RA patients, getting different therapeutic regimens,during the 2-year follow-up.

Disclosure of Interest: None declared
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THU0133 SERUM PENTRAXIN-3 IN THE ASSESSMENT OF CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

B. Targonska-Stepniak, M. Piotrowski, R. Zwolak, M. Majdan. *Department of Rheumatology and Connective Tissue Diseases, Medical University of Lublin, POLAND, Lublin, Poland*

Background: Rheumatoid arthritis (RA) is associated with the increased cardiovascular (CV) morbidity and mortality due to accelerating, progressive atherosclerosis. The chronic, systemic inflammatory process is responsible for both joint damage and increased CV risk in RA patients. Pentraxin 3 (PTX3) is an inflammatory marker, a member of long pentraxin superfamily, supposed to be involved in inflammatory process as well as in atherosclerosis.
Objectives: The goal of the study was to assess the role of PTX3 as an inflammatory marker in patients with RA and to evaluate the relationship between PTX3 and CV risk markers [carotid intima-media thickness (cIMT), QTc distance (dQTc), lipid profile].
Methods: The study group consisted of 72 consecutive RA patients, 60 (83,3%) female and 12 male (16,7%), with the mean (SD) age 53,4 (10,29) (range 21–71) and disease duration 16,8 (10,3) years (range 2–49). The activity of RA was estimated by clinical examination with the disease activity score in 28 joints (DAS28). Remission or low disease activity was observed in 35 (48,6%) patients; moderate or high disease activity (DAS28 >3,2) in 37 (51,4%) patients. Disease modifying antirheumatic drugs (DMARDs) used in the treatment included: methotrexate 61 (84,7%) patients, chlorochine or hydroxychlorochine 9 (12,5%), leflunomide 4 (5,6%), cyclosporine 1 (1,4%) patient. The majority of patients 54 (75%) were treated with biological DMARDs, currently or in the past.
Results: The mean (SD) PTX3 concentration in RA patients was 4,57 (2,83) ng/ml (range 1,43- 16,07). The mean (SD) cIMT value was 0,86 (0,2) mm (range 0,43–1,77). There were 19 (26,4%) RA patients with advanced atherosclerosis (presence of atherosclerotic plaques).
The positive, significant correlations were found between PTX3 concentration and other inflammatory markers: C-reactive protein (CRP) (R=0,5), ESR (R=0,46) and white blood cell count (WBC) (R=0,41). PTX3 concentration was also correlated with clinical disease activity markers: DAS28 value (R=0,41), as well as with tender joint count (TJC) (R=0,01), swollen joint count (SJC) (R=0,009), patient's global assessment of the disease activity (R=0,02).
The mean (SD) PTX3 concentration was significantly higher in patients with moderate/high RA activity in comparison with remission/low disease activity [5,56 (3,29) vs 3,48 (1,71) ng/ml, p=0,001] and in patients anti-CCP positive compared with anti-CCP negative [4,57 (2,58) vs 3,02 (0,85) ng/ml, p=0,04].
The mean (SD) PTX3 concentration was significantly higher in patients with definite atherosclerosis (cIMT >0,9 mm) than in patients with subclinical or no atherosclerosis [5,77 (3,02) vs 3,99 (2,58) ng/ml, p=0,04], as well as in patients with atherosclerotic plaques in comparison with no plaques (6,18 (2,83) vs 4,02 (2,64) ng/ml, p=0,0006).
There was a negative correlation between PTX3 and dQTc (R= -0,33, p=0,007).
Conclusions: The results of the study suggest a twofold role of PTX3:
1. an inflammatory marker of the joint disease activity
2. a biomarker indicating intensity of atherosclerosis, estimated by greater cIMT value and the presence of atherosclerotic plaques. The negative correlation between PTX3 and dQTc suggests the increased risk of sudden cardiac death due to shortening of dQTc.

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THU0134 INTERSTITIAL LUNG DISEASE AND RHEUMATOID ARTHRITIS. MULTICENTER STUDY WITH TOCILIZUMAB

C. Fernández-Díaz [1], J. Narvaez-García [2], M. Martín-López [3], P. Rubio-Muñoz [4], S. Castañeda-Sanz [5], N. Vegas-Revenga [1], L. Dominguez-Casas [1], V. Calvo-Rio [1], M. Gonzalez-Gay [1], R. Blanco [1]. *[1] Rheumatology, Hospital Universitario Marques de Valdecilla, Santander; [2] Rheumatology, Hospital Universitario Belvitge, Barcelona; [3] Rheumatology, Hospital 12 de Octubre, Madrid; [4] Rheumatology, Hospital Universitario Germans Trias i Pujol, Barcelona; [5] Rheumatology, Hospital la Princesa, Madrid, Spain*

Background: Interstitial Lung Disease (ILD) is a severe extraarticular manifestation of rheumatoid arthritis (RA). AntiTNFα drugs and conventional disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate (MTX) have been involved in the development of ILD. IL6 has been implicated in the pathogenesis of ILD (Kobayashi J et al). However, a fatal case of exacerbation of ILD has been described with tocilizumab (TCZ) (Kawashiri SY el at).
Objectives: Our aim was to assess the efficacy and safety of TCZ in ILD associated with AR.
Methods: Multicenter study of RA patients with ILD treated with TCZ. ILD was diagnosed by high-resolution computed tomography (HRCT). TCZ was used at standard dose (8 mg/k/iv/4 weeks). We have analyzed the following variables: a) 1-point change in the degree of dyspnea according to the Modified Medical Research Council (MMRC); b) Forced Vital Capacity (FVC) improvement ≥10%; and improvement ≥10% in DLCO; c) HRCT, and d) joint assessment (DAS28 score).
Results: We studied 12 patients (9 women/3 men) with ILD related to RA.

The mean age±SD was 57.1±16.1 years. The mean evolution of RA was 9±5.8 years. The patients had previously received the following DMARDs; MTX (n=12), leflunomide (LFN) (8) sulfasalazine (SSZ) (3) hydroxichloroquine (HCQ) (1) azathioprine (AZA) (2), gold salts (2). In addition, 11 patients had previously received biological drugs: adalimumab (4) anakinra: (1), etarnecept (4), rituximab (4), infliximab (1), certolizumab (1), abatacept (1). RA was seropositive in 11 cases (92%). Besides HRCT, the diagnosis of ILD was confirmed by biopsy in 4 patients. In 2 patients ILD was drug-related: MTX (n=2). TCZ was prescribed in monotherapy (n=8) or combined with other DMARDs (4). These DMARDs were: LFN (2), MTX (1), AZA (1). In many patients the dyspnea and DLCO remain stable (Table). After a follow-up of 12 months, 2 patients withdrew TCZ, 1 patient for ILD worsening and 1 patient for joint inefficacy.

Table 1

	Baseline	3th month	6th month	12th month
MRC, n (%)		11	8	11
– No change		11 (100)	7 (87)	8 (73)
– Improvement		0	0	2 (18)
– Worsening		0	1 (13)	1 (9)
FCV, n (%)		2	5	9
– No change		2 (100)	5 (100)	6 (67)
– Improvement		0	0	2 (23)
– Worsening		0	0	1 (12)
DLCO, n (%)		2	4	9
– No change		1 (50)	3 (75)	9 (100)
– Improvement		0	0	0
– Worsening		1 (50)	1 (25)	0
HRTC, n (%)		0	2	10
– No change			1 (50)	7 (70)
– Improvement			0	0
– Worsening			1 (50)	3 (30)
DAS28 – *mean*	4.46±1.40	3.35±1.19	3.23±1.04	2.98±0.95
CRP (mg/dl) – *mean*	3.23±2.96	1.11±0.98	1.48±0.95	1.15±0.84
ESR (mm/1st h) – *mean*	45.17±28.84	16.16±10	16.16±11.41	17.47±25.45

Conclusions: In our knowledge, this is the largest series that assess the EPID associated with RA treated with TCZ. We observed that in many cases pulmonary involvement remains stable.

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THU0135 THE COURSE OF LOWER EXTREMITY FUNCTION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS OVER THE FIRST FIVE YEARS

M. Mellblom Bengtsson[1], C. Book[1,2], S. Hagel[3,4], L.T. Jacobsson[5], C. Turesson[1,2]. *[1]Department of Rheumatology, Skåne University Hospital; [2]Rheumatology, Department of Clinical Sciences, Malmö, Lund University, Malmö; [3]Rheumatology, Department of Clinical Sciences, Lund, Lund University; [4]Department of Rheumatology, Skåne University Hospital, Lund; [5]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy at Gothenburg University, Gothenburg, Sweden*

Background: Rheumatoid arthritis (RA) frequently involves joints of the feet and the knees. Disability related to arthritis in the lower extremities has a major impact in many patients, but has not been extensively studied.

Objectives: To investigate lower extremity function in early RA, using validated tests, and to assess its relation to other disease parameters.

Methods: Consecutive patients with early RA (symptom duration ≤12 months) in an inception cohort from a well-defined area were followed according to a structured protocol, with visits at inclusion and after 1, 2 and 5 years. Lower extremity function was investigated using the Index of Muscle Function (IMF) (1), a validated battery of tests by which the patient's general ability, muscle strength, muscular endurance and balance/coordination are assessed by a physiotherapist. The scores on the subscales are added for a total IMF score (IMF total) of 0–40. A subscore of the Health Assessment Questionnaire Disability Index (HAQ-DI), based on the 10 questions that are mainly dependent on function of the lower extremities (the HAQ-DI-LE (2)) was calculated, as well as a modified HAQ-DI-LE (mHAQ-DI-LE) that included only the three HAQ-DI domains in which all questions relate mainly to the lower extremities. Changes in the IMF total score and subtest scores between visits were analyzed using the Wilcoxon signed rank test. Correlations between disease parameters were assessed using Spearman's rank test.

Results: A total of 106 patients (67% women, mean age 61 years, mean baseline DAS28 4.4, median baseline HAQ-DI 0.75) were included. Data on IMF total were available for 100, 89 and 67 patients at the 1, 2 and 5-year visits. Lower extremity function improved from baseline to the 1-year visit (IMF total median 10; interquartile range (IQR) 4–16 vs. 7; IQR 3–12) (p=0.01). This was followed by a decline in lower extremity function, in particular between the 2-year and 5-year visits (IMF total median 8 (IQR 3–13) vs 9.5 (IQR 3.75–18.25); p=0.001). This was mainly due to worsening in test results for muscle strength (median 4 (IQR 1–6) vs 5 (IQR 2–9); p=0.001) and for balance/coordination (median 2 (IQR 0–4) vs 3 (IQR 2–6); p=0.001). At baseline, IMF total correlated with HAQ-DI-LE (r=0.46), mHAQ-DI-LE (r=0.49) and HAQ-DI (r=0.40) (all p<0.001), whereas there were weaker correlations with CRP (r=0.24; p=0.02) and DAS28 (r=0.28; p=0.004). There were consistent correlations between IMF total and HAQ-DI-LE, mHAQ-DI-LE and HAQ-DI at all time points, but no significant correlations for IMF total with CRP and DAS28 at the 2-year visit.

Conclusions: In early RA, there was improvement in lower extremity function during the first year, followed by a gradual decline, possibly explained by lack of complete disease control and aging. Tests of muscular function in the lower extremities may reveal aspects of RA disease severity that are not fully captured by standard disease activity measures, and may add important information regarding functional loss.

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THU0136 NESFATIN-1 EXPRESSION IS ASSOCIATED WITH REDUCED ATHEROSCLEROTIC DISEASE RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

C. Robinson[1], L. Tsang[1], A. Solomon[1], A. Woodiwiss[1], S. Gunter[1], H.-C. Hsu[1], G. Norton[1], A. Millen[1], P. Dessein[1,2]. *[1]Cardiovascular Pathophysiology and Genomic Research Unit, School of Physiology, University of the Witwatersrand, Johannesburg, South Africa, Johannesburg, South Africa; [2]Rheumatology Division, Universitair Hospital Brussel, Brussels, Belgium*

Background: Nesfatin-1 comprises a peptide that is involved in appetite suppression, energy homeostasis and fluid regulation, and was recently documented to participate in a range of cardiometabolic pathways (1,2). There is currently a need for the identification of novel biomarkers in the elucidation of CVD risk and its stratification in persons with rheumatoid arthritis (RA). The role of nesfatin-1 in cardiovascular disease risk among RA patients is uncertain.

Objectives: We investigated the potential impact of nesfatin-1 on subclinical cardiovascular disease manifestations in patients with RA by determining the associations of nesfatin-1 concentrations with atherosclerosis and circulating levels of matrix metalloproteinase (MMP)-2 that mediates plaque stability and those of MMP-3 and MMP-9 that cause plaque vulnerability.

Methods: Nesfatin-1 concentrations were measured in 236 (114 black; 122 white) RA patients. Relationships of nesfatin-1 concentrations with ultrasound determined carotid intima-media thickness (cIMT) and plaque and MMP levels were identified in confounder adjusted multivariate regression models.

Results: Nesfatin-1 concentrations were inversely associated with c-IMT (β (SE) = -0.022 (0.008), p=0.00) and directly with MMP-2 levels (β (SE) =0.117 (0.031), p=0.00). After adjustment for conventional risk factors and RA characteristics, these associations persisted (c-IMT: β (SE) = -0.017 (0.008), p=0.04; MMP-2: β (SE) =0.116 (0.033), p=0.00). Patient characteristics did not influence the nesfatin-1-to-cIMT relation (interaction p≥0.7). By contrast, the Disease Activity Score in 28 joints (DAS28) and Clinical Disease Activity Index impacted the nesfatin-1-to-cIMT association (interaction p=0.04 and 0.02, respectively). Nevertheless, in stratified analysis, nesfatin-1 concentrations were related to those of MMP-2 in patients with no or mild (β (SE) =0.148 (0.054), p=0.00) and moderate or high disease activity (β (SE) =0.086 (0.041), p=0.04) as determined by DAS28 (cut-off value 3.6) as well as by CDAI (cut-off value =10) (β (SE) =0.130 (0.048), p=0.00 and 0.107 (0.046), p=0.02), respectively).

Conclusions: Nesfatin-1 concentrations are consistently associated with a reduced atherosclerosis burden and increased MMP-2 levels in patients with RA.

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THU0137 IMPACT OF PERIODONTAL AND RHEUMATIC DISEASE MARKERS ON FIRST-DEGREE RELATIVES OF PATIENTS WITH RHEUMATOID ARTHRITIS ACCORDING TO AGE GROUP

C. Romero-Sanchez[1,2], S. Giraldo[3], J. De-Avila[1], M.A. Cano-Bermuedez[1], L. Chila-M.[1], J. Bello-Gualtero[2], P. Chalem[4], W. Bautista[3], J. Londono[5], C. Pacheco-Tena[6], G. Lafaurie[1], R. Valle-Oñate[7]. *[1]Unit of Oral Basic Investigation/School of Dentistry, Universidad El Bosque; [2]Department of Rheumatology and Inmunology, Hospital Militar Central, Bogotá, Colombia; [3]School of Medicine, Universidad Militar Nueva Granada; [4]Departamento de Reumatologia, Fundacion Instituto de Reumatologia Fernando Chalem, Bogotá D.C; [5]Spondyloarthropaty Group, Rheumatology Universidad de la Sabana, Chia, Colombia; [6]Departamento de Reumatologia, Investigacion y Biomedicina S.C., Chihuahua, Mexico; [7]Departamento de Reumatologia, Hospital Militar Central, Bogotá, Colombia, Bogotá D.C., Colombia*

Background: Rheumatoid arthritis (RA) and periodontal disease (PD) have