POS1441

SYMPTOMS CHARACTERISTICS OF SEROPOSITIVE INDIVIDUALS AT-RISK FOR DEVELOPING RHEUMATOID ARTHRITIS ARE VERSATILE AND COMPARABLE TO THOSE IN PEOPLE WITH EARLY RHEUMATOID ARTHRITIS

P. Studenic^{1,2}, A. Circumaru^{1,3}, D. Aletaha², K. Chatzidionysiou^{1,4}, A. Hensvold^{1,3}, A. Catrina^{1,4}. ¹Karolinska Institute, Department of Medicine (Solna), Division of Rheumatology, Stockholm, Sweden; ²Medical University of Vienna, Department of Internal Medicine 3, Division of Rheumatology, Wien, Austria; ³Academic Specialist Center - Stockholm Health Care Services, Center for Rheumatology, Stockholm, Sweden; ⁴Karolinska University Hospital, Rheumatology Unit, Stockholm, Sweden

Background: The symptom burden of typical rheumatoid arthritis (RA) symptoms in those at risk for developing RA - positive for anti-citrullinated peptide antibodies (ACPA) and musculoskeletal complaints - has not been explored.

Objectives: To evaluate patient-reported symptoms in individuals at-risk to develop RA in comparison to people with newly diagnosed, early seropositive RA.

Methods: Two datasources from the region of Stockholm were used: The RISK RA cohort follows up ACPA positive individuals with arthralgia, but without signs of joint inflammation in a structured program over 3 years. The baseline visit of this cohort was used. Patients with early seropositive (ACPA and/or rheumatoid factor positive) RA (symptom duration of 12 months maximum) reported in the Swedish Rheumatology Quality Register (SRQ) at their closest visit to their diagnosis date before receiving DMARD treatment have been identified. At-risk individuals were matched 1:3 by sex and age using the nearest neighbour method utilizing Mahalanobis distance, corrected for sample bias and exact matches on sex. Effect estimates of being at-risk compared to early RA for pain, patient global (GH), fatigue (all visual analogue scales), health assessment questionnaire (HAQ), TJC28 and the EuroQoL-5D (EQ5D; range: 0-1) have been derived. Propensity score matching was used as sensitivity analyses.

Results: A total of 223 individuals at risk for developing RA were compared to 820 matched early RA patients. The summary of distribution of variables and effect estimates of differences between at-risk and early RA individuals are shown in the Figure 1. At-risk individuals show 24mm of lower pain scores than early RA. This difference is even less (-17mm, 95%CI: -24 to -11) when the estimate is additionally matched for the number of tender joints. The TJC28 was on average 5.4 joints lower than in early RA patients. People at-risk show 22mm lower GH scores (rate themselves better) and 17mm lower fatigue scores than early RA patients. Fatigue was scored highest (mean:35mm, 95%CI: 30 to 29) among the three VAS. HAQ was on average lower by 0.6 points in at-risk individuals and EQ5D showed 0.24 higher index-values, outlining a better health status. Still the mean EQ5D in at-risk individuals was only 0.74 (95%CI: 0.71 to 0.77), which is lower than average values of an age-matched general population (0.92 to 0.96). Sensitivity analyses revealed similar results.

Figure 1. Boxplots of pain, global health, fatigue, TJC28, EQ5D and HAQ, separately displayed for people with early seropositive RA and individuals at-risk. Population effect estimates (all $p < 0.001$) comparing at-risk to early RA are provided for every pair, with 95% confidence interval in brackets.

Conclusion: Not surprisingly, individuals at risk for RA report less symptom burden than early diagnosed RA patients. However, these differences only range around minimal clinically important differences and for fatigue even below, which stresses the need for medical attention and management strategies for symptomatic at-risk individuals.

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Validation of outcome measures and biomarkers

POS1442

THE SUBGROUP OF ACPA-NEGATIVE RHEUMATOID ARTHRITIS PATIENTS ACHIEVING SUSTAINED DMARD-FREE REMISSION IS CHARACTERIZED BY A DIFFERENT RESPONSE IN SEROLOGICAL MARKERS WITHIN THE FIRST YEAR OF DMARD-INITIATION

M. Verstappen¹, A. Van der Helm - van Mil^{1,2}. ¹Leiden University Medical Center, Rheumatology, Leiden, Netherlands; ²Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands

Background: Whilst ~40% of ACPA-negative RA-patients achieve sustained DMARD-free remission (SDFR; the sustained absence of synovitis after DMARD-cessation), the biological pathways involved in SDFR-development are incompletely understood. Previously, high baseline levels of MMP-3, SAA and CRP were found in ACPA-negative RA-patients achieving SDFR. Differences in biomarker levels might reflect distinct underlying biological pathways leading towards disease resolution in this subgroup of ACPA-negative RA-patients. Subsequently, the course of specific biomarkers after treatment-initiation could attain more insight in the understanding of SDFR-development in ACPA-negative RA.

Objectives: We explored whether the response of specific biomarkers after treatment-initiation could increase the understanding of SDFR-development in ACPA-negative RA.

Methods: One-hundred-thirty-one consecutive ACPA-negative RA-patients were studied on SDFR-development during (median) 7.2-years follow-up. Twelve biomarkers (SAA/CRP/MMP-1/MMP-3/resistin/leptin/IL-6/TNF-R1/YKL-40/EGF/VEGF/VCAM-1) were measured at diagnosis and 1-, and 2-years after DMARD-initiation and compared between patients achieving and not achieving SDFR. To extend on previous findings on baseline levels, correlations between baseline levels and change in levels within year-1 were determined using Spearman's rho (ρ).

Results: RA-patients that achieved SDFR ($n=63$) were characterized by a stronger decline in MMP-1, MMP-3, SAA and CRP in the first 12-months after DMARD-start, compared to RA-patients not achieving SDFR. MMP-1 and MMP-3 declined 1.30-times (95%CI: 1.08-1.57) and 1.44-times (95%CI: 1.00-2.06) stronger in SDFR-patients. In SAA and CRP, this decline was 2.12-times (95%CI: 1.08-4.14) and 2.24-times (95%CI: 1.16-4.35) stronger. Baseline levels of MMP-3, SAA and CRP and strongly correlated with decline in 12-months; ρ -0.6991, ρ -0.9205 respectively ρ -0.9008. RA-patients with high baseline levels characterized the subgroup with the strongest decline in biomarker levels in the first year after DMARD-initiation.

Conclusion: The subgroup ACPA-negative RA-patients achieving SDFR are characterized by higher baseline levels and a stronger serological response of MMP-3, SAA and CRP after DMARD-initiation. Because MMP-3 and SAA are expressed by fibroblast-like synoviocytes, these cells may differ in RA-patients achieving disease resolution; molecular studies on synovial tissue could be a next step.

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POS1443

RELATIONSHIP BETWEEN FIBRINOGEN TO ALBUMIN RATIO AND DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

M. Liu¹, Y. Huang¹, Z. Huang¹, Q. Huang¹, T. W. Li¹. ¹Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China

Background: Systemic lupus erythematosus (SLE) is a systemic inflammatory autoimmune disease characterized by excessive production of immune complexes and proinflammatory cytokine. Low complement, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been used as inflammatory biomarkers to assess the disease activity of SLE. Recently, the fibrinogen to albumin ratio (FAR) has emerged as an effective indicator to reflect the systemic inflammation in many diseases. However, the role of FAR in SLE has been scarcely studied.

Objectives: This study was to investigate the association between FAR and SLE Disease Activity Index 2000 (SLEDAI-2K) in SLE.

Methods: This retrospective study included 74 SLE patients and 79 age- and sex-matched healthy subjects. According to the SLEDAI-2K score, SLE patients were divided into Group 1 with a score ≤ 9 (patients with mild disease activity, $N = 41$) and Group 2 with a score > 9 (patients with moderate to severe disease activity, $N = 33$). Neutrophil, lymphocyte, monocyte, platelet, albumin, fibrinogen, NLR, PLR, monocyte to lymphocyte ratio (MLR), FAR, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complement 3 (C3), complement 4 (C4) and SLEDAI-2K were collected. Receiver operation characteristic (ROC) curves were conducted to discriminate SLE patients from healthy controls and SLE patients with different disease activity. Correlations between the inflammatory markers and SLEDAI-2K were analyzed.

Results: FAR, NLR, PLR, MLR and fibrinogen in SLE patients were higher compared to those of the healthy controls ($P < 0.05$), while albumin was lower ($P < 0.05$). Patients in Group 2 had higher levels of FAR, NLR, PLR, fibrinogen and CRP than those in Group 1 ($P < 0.05$) except MLR ($P = 0.579$) and ESR ($P = 0.130$), albumin and C3 were lower ($P < 0.05$). Furthermore, FAR were higher in SLE patients with nephritis than those without nephritis ($P = 0.009$). The ROC curve for differentiating SLE patients from healthy individuals showed that the area under curve (AUC) of FAR (0.801, 95%CI: 0.728 - 0.874) and albumin (0.833, 95%CI: 0.764-0.903) were higher than NLR (0.798, 95%CI: 0.725 - 0.871), PLR (0.680, 95%CI: 0.588 - 0.771), MLR (0.785, 95%CI: 0.712 - 0.859) and fibrinogen (0.645, 95%CI: 0.556 - 0.733). Besides, the ROC curve for predicting the disease activity of SLE patients indicated that the AUC of FAR (0.911, 95%CI: 0.842 - 0.980) was higher than NLR (0.697, 95%CI: 0.574 - 0.821), PLR (0.695, 95%CI: 0.571 - 0.820), MLR (0.553, 95%CI: 0.415 - 0.691), fibrinogen (0.718, 95%CI: 0.590 - 0.847), CRP (0.672, 95%CI: 0.540 - 0.803), ESR (0.640, 95%CI: 0.510 - 0.770), C3 (0.644, 95%CI: 0.515 - 0.773), C4 (0.544, 95%CI: 0.407 - 0.681) and albumin (0.894, 95%CI: 0.819 - 0.969). FAR was positively correlated with SLEDAI-2K ($r = 0.682$, $P < 0.001$), yielding a highest relevance than other inflammatory parameters.

Conclusion: FAR was significantly elevated in SLE patients compared with healthy subjects and related with the disease activity of SLE. FAR might be a useful inflammatory index to evaluate disease activity in patients with SLE.

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POS1444 ADOPTION OF DIGITAL MANIKINS TO SELF-REPORT PAIN: A SYSTEMATIC REVIEW

S. Mustafa Ali¹, R. Lee¹, A. Chiarotto², J. Mcbeth¹, S. Van der Veer³, W. Dixon¹.
¹University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom; ²Erasmus University Medical Centre, Department of General Practice, Rotterdam, Netherlands; ³University of Manchester, Centre for Health Informatics, Manchester, United Kingdom

Background: Chronic pain is common in rheumatic and musculoskeletal conditions, and a major driver of disability worldwide. Knowledge gaps exist with respect to correct estimates of chronic pain [1], what causes it and how best to manage it [2]. To address this, researchers need validated methods to measure pain in large, representative populations. Though many authors have recognised the potential benefits of paper-based and digital pain manikins [3]–[5], it is unknown to what extent studies have adopted digital manikins as a data collection tool.

Objectives: The objective of our review was to identify and characterise published studies that have used digital pain manikins as a data collection tool.

Methods: We systematically searched six electronic databases, including Medline, CINAHL, Embase, Scopus, IEEE Xplore digital library, ACM Digital Library, on 3-4 of November 2020 by using a pre-defined search strategy. We included a study in our review if it used a digital manikin for self-reporting any pain aspect (e.g., intensity, type) by people suffering from pain, and if its full text was published in English. We conducted this review by following the PRISMA reporting guidelines and conducted a descriptive synthesis of findings, including manikin-derived outcome measures.

Results: Our search yielded 4,685 unique studies. After full text screening of 705 articles, we included 14 studies in our review. Most articles were excluded because they used either paper-based manikins or didn't include enough details to determine that the manikin was digital ($n=386$). The majority of included studies were published in Europe ($n=11$). Most studies collected data on a manikin once ($n=11$); from people with pain conditions ($n=9$); and in clinical settings ($n=9$). There was only one study that collected digital pain manikin data in a large sized (i.e., ~20,000) population-based survey.

In most studies participants shaded any painful area on manikin ($n=9$) and did not enable participants to record location-specific pain aspects ($n=11$). None of the manikins enabled participants to record location-specific pain intensity. Pain distribution (i.e. number or percentage of pre-defined body areas or locations experiencing pain) and pain extent (i.e. number or percentage of shaded pixels) were commonly used manikin-derived outcome measures. In six studies, a heat map was used to summarise the extent of pain across the population.

Conclusion: Digital pain manikins have been available since the 1990s but their adoption in research has been slow. Few manikins enabled location-specific pain recording suggesting that the digital nature of the manikin is not yet fully utilised. Future development of a validated digital pain manikin supporting self-reporting of the location and intensity of pain, usable across any device and screen size, may increase uptake and value.

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POS1445 RETINOL BINDING PROTEIN 4 AS AN ACUTE PHASE REACTANT AND BIOMARKER IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER AND AMYLOIDOSIS COMPARED TO INFECTIONS

N. Koca¹, R. Deniz¹, M. Erdugan¹, Y. Yalçinkaya¹, B. Artim-Esen¹, M. L. Ocal¹, M. Inanc¹, A. Gül¹.
¹Istanbul Faculty of Medicine, Istanbul University, Division of Rheumatology, Department of Internal Medicine, Istanbul, Turkey

Background: Retinol binding protein 4 (RBP4) is a plasma retinol transporter that transports retinol from liver to periphery. RBP4 has been studied as a biomarker in metabolic and neoplastic conditions, however its association with inflammation is not clear. Serum amyloid A (SAA), another retinol binding protein, has been known as a sensitive biomarker of inflammation in familial Mediterranean fever (FMF) and other autoinflammatory disorders. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and SAA are commonly used as acute phase reactants, but they are not successful in differentiating non-infectious inflammatory conditions from infections.

Objectives: We aimed to evaluate the potential of serum RBP4 as a biomarker of acute phase response and to determine its performance in differentiation of inflammation of patients with FMF and AA amyloidosis from infections.

Methods: A total of 169 participants in 5 groups, consisting of FMF ($n = 60$), FMF with AA amyloidosis ($n = 58$), non-FMF AA amyloidosis ($n = 23$), infections ($n = 10$, 3 pneumonia, 3 sepsis, 1 pyelonephritis, 1 fungal infection, 1 cellulitis, 1 disseminated zoster), and healthy controls (HC) ($n = 18$), were included and evaluated cross sectionally. Hemogram and serum CRP, ESR, SAA, ferritin, creatinine, AST, ALT, albumin levels were recorded from the patient charts. FMF and FMF + amyloidosis patients were evaluated during attack-free period. Serum RBP4 levels were investigated by ELISA (Elabscience, USA). Mean values and relative changes compared to healthy controls were evaluated for SAA, CRP, RBP4 levels in all groups.

Results: Serum RBP4 level was found to be higher in FMF group compared to the patients with infection ($p = 0.002$) and HC ($p < 0.001$) as well as in patients with amyloidosis. Compared to HC, 47%, 28% and 27% increase was observed in mean RBP4 levels in FMF, FMF + amyloidosis and non-FMF amyloidosis patients, despite no significant change in patients with infections. However, CRP and SAA elevations were much more prominent in patients with infections (58 and 134 times, respectively) compared to the patients with FMF (13 and 35 times, respectively), FMF + amyloidosis and non-FMF amyloidosis (Table 1). There was no significant difference in RBP4 levels between FMF, FMF-amyloidosis and non-FMF amyloidosis groups. CRP, ESR, ferritin and SAA levels were higher in the infection group compared to HCs.