References:
[1] Xu D, Jiang HR, Li Y, et al. IL-33 exacerbates autoantibody-induced arthritis. J Immunol. 2010;184(5):2620–2626.
[2] Matsuyama Y, Okazaki H, Tamemoto H, et al. Increased levels of interleukin 33 in sera and synovial fluid from patients with active rheumatoid arthritis. J Rheumatol. 2010;37(1):18–25.
[3] Schmitz J, Owyang A, Oldham E, et al. IL-33, an interleukin-1-like cytokine that signals via the IL-1 receptor-related protein ST2 and induces T helper type 2-associated cytokines. Immunity. 2005;23(5):479–490.
[4] Alberti KG, Zimmet P, Shaw J. Metabolic syndrome–a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med. 2006;23(5):469–480.
[5] Steinbrocker O, Traeger CH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. JAMA 1949;140:659–62.
[6] Kunes P, Holubcová Z, Kolácková M, Krejsek J. The counter-regulation of atherogenesis: a role for interleukin-33. Acta Medica (Hradec Kralove). 2010;53(3):125–129.
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FRI0113 VALIDATION AND RESULTS OF THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS (SPARRA) QUESTIONNAIRE

M.V. Beers-Tas[1], M. Ter Wee[2], B. Maat[1], W. Hoogland[1], A. Hensvold[3], A. Catrina[3], E. Mosor[4], A. Finckh[5], D. Courvoisier[6], K. Raza[7], D.V. Schaardenburg[1]. *[1]Amsterdam Rheumatology and immunology Center, Reade; [2]Amsterdam Rheumatology and immunology Center, VUMC, Amsterdam, Netherlands; [3]Rheumatology, Karolinska university, Stockholm, Sweden; [4]Rheumatology, Section for Outcomes Research, CeMSIIS, Medical University of Vienna, Vienna, Austria; [5]Rheumatology; [6]University hospital of Geneva, Geneva, Switzerland; [7]Rheumatology, Institute of Inflammation and Ageing, Birmingham, United Kingdom*

Background: A range of symptoms can be present in persons at risk of rheumatoid arthritis (RA). However, information on the nature, location, timing, severity and predictive value of these symptoms is largely lacking. The Symptoms in Persons At Risk of Rheumatoid Arthritis (SPARRA) questionnaire has been developed with support from EULAR, informed by data from a qualitative study[1] and with input from patient research partners.
Objectives: To test the psychometric properties of the SPARRA questionnaire in an international group of arthralgia patients at risk of RA and to quantify these symptoms.
Methods: The SPARRA questionnaire contains questions about presence, severity, impact and location of 13 symptoms. 240 individuals (69% rheumatoid factor and/or ACPA positive, 23% seronegative with clinically suspect arthralgia and 8% first degree family members of patients with RA) completed the questionnaire in the Netherlands (N=125), United Kingdom (N=70), Sweden (N=15), Austria (N=11) and Switzerland (N=19). Individuals had no history or presence of clinically diagnosed arthritis at the time of first physical examination. Reliability (test-retest) and validity (face, content and construct validity) were tested.
Results: Face validity was tested by a group of experts on the at-risk phase of RA and feedback on the questionnaire was asked and received from 30 arthralgia patients, leading to only minor comments. The test-retest within 7–14 days (N=51) showed moderate to good agreement (kappa mean 0.565, range 0.309–1; agreement mean 71%, range 59–100%). The content validity was high, in line with the fact that the items were derived from a qualitative study in seropositive arthralgia patients. In contrast, the construct validity (relation to visual analog scale scores (VAS) for pain and well-being) was low (R-square 0.040–0.199), suggesting that the questions measure different elements in different time frames and grasp symptom content not captured with regular VAS pain/well-being. Most symptoms were present in a high percentage of individuals, with pain, stiffness and fatigue as the most common ones. When a symptom was present, it was usually experienced as moderate to severe, and with moderate impact. ACPA positive individuals reported lower presence of symptoms then ACPA negative individuals (mean 47% for ACPA-positive (N=118), 41% for only RF positives (N=53) and 59% in seronegative individuals (N=69)), but functional impact was higher in ACPA positive individuals (51%, versus 42% in seronegatives, NS). Note that the inclusion criteria for the seronegative individuals was presence of symptoms.
Conclusions: This study provides evidence of good psychometric properties of the SPARRA questionnaire, except for low construct validity. This means the questionnaire adds information to currently available clinical measures in persons at risk of RA. Future studies are needed to evaluate whether SPARRA data can help to improve the prediction of RA.
References:
[1] Stack, Rheumatology 2014.
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FRI0114 ALLOGRAFT INFLAMMATORY FACTOR 1 (AIF1) POLYMORPHISMS RS4711274 (G/A) AND RS2269475 (C/T) MAY PREDICT ETANERCEPT PLUS METHOTREXATE RESPONSE IN FRENCH CAUCASIAN PATIENTS WITH RHEUMATOID ARTHRITIS

D.F. Azzouz[1], M. El Haddad[1], S. Kanaan[1], N. Balandraud[1,2], M. Martin[1], C. Picard[3], J. Roudier[1,2], I. Auger[1], N.C. Lambert[1]. *[1]INSERM UMRs1097; [2]Rheumatology, AP-HM; [3]HLA Laboratory, Etablissement Français du Sang, Marseille, France*

Background: Several risk loci for Rheumatoid Arthritis (RA) have been identified by Genome Wide Association Studies (GWAS), but they do not include Allograft Inflammatory Factor 1 (AIF1). Nevertheless, a few studies have shown that AIF1 rs2269475 (C/T) is associated with RA[1,2].
Objectives: We propose 1) To examine associations in French Caucasian patients with RA, of the seven most described AIF1 SNPs; 2) To study their linkage disequilibrium with HLA-DRB1 alleles; 3) To evaluate whether AIF1 single nucleotide polymorphisms (SNPs) could predict first line treatment responses in RA.
Methods: We amplified the AIF1 gene region containing the 7 SNPs and sequenced PCR products on a total of 469 individuals, including 95 Anti-Citrullinated Protein Antibody (ACPA) positive RA patients, 146, patients with scleroderma, 132 healthy controls and 96 additional healthy controls selected from a large database of volunteer bone marrow donors (VBMD) for carrying at least one RA-associated allele. Patients and controls were HLA-DRB1 genotyped. Patients with RA were divided into 2 groups, a first group called "*non responders*" was defined as patients who did not respond to first-line methotrexate (MTX) combined with Etanercept and a second group called "*good responders*" was defined as patients who did respond to methotrexate combined with Etanercept.
Results: Two SNPs were associated with RA: *rs4711274 (G/A)* and *rs2269475 (C/T)*. The frequency of minor allele carriers was respectively 37% (A) and 36% (T) in patients with RA versus 18% among controls (p=0.0014 and p=0.001). Furthermore, patients with RA-associated HLA-DRB1 alleles carried more often minor alleles for both SNPs (p=0.0005). Preliminary clinical data show that 56% of non-responders (N=16) carried the minor alleles of both rs4711274 and rs2269475 compared to only 21% of good responders (N=24, p=0.02).
Conclusions: AIF is an inflammation-responsive protein encoded within the HLA class III region on chromosome 6 (6p21.3). As already described in British and Polish Caucasians, we found a significant AIF1 Rs2269475 association with RA. We also found an association with Rs4711274 in linkage disequilibrium with the former. The increased frequency of minor AIF1 alleles in RA was not associated with a particular HLA-DRB1 allele, but to any HLA-DRB1 allele carrying the shared epitope.
Finally, patients who failed to respond to Etanercept and MTX carried more often minor alleles of the 2 described AIF1 SNPs.
Further analysis on a larger groups of patients is required to confirm whether AIF1 SNPs can predict response to therapy with Etanercept and Methotrexate.
References:
[1] Harney SM, Vilarino-Guell C, Adamopoulos IE, Sims AM, Lawrence RW, et al. (2008) Fine mapping of the MHC Class III region demonstrates association of AIF1 and rheumatoid arthritis. Rheumatology 47: 1761–1767.
[2] Pawlik A, Kurzawski M, Szczepanik T, Dziedziejko V, Safranow K, et al. (2008) Association of allograft inflammatory factor-1 gene polymorphism with rheumatoid arthritis. Tissue antigens 72: 171–175.
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FRI0115 EVER-SMOKING IS ASSOCIATED WITH DISEASE SEVERITY AND OPIOID USE IN RHEUMATOID ARTHRITIS

A. Karellis[1], E. Rampakakis[1,2], J.S. Sampalis[1,2], M. Cohen[3], M. Starr[3], P. Ste-Marie[4], Y. Shir[4], M. Ware[4], M.-A. Fitzcharles[3,4]. *[1]JSS Medical Research, St-Laurent; [2]Jewish General Hospital; [3]Rheumatology; [4]Alan Edwards Pain Management Unit, McGill University Health Centre, Montreal, Canada*

Background: Cigarette smoking, both current and past, is a risk for incident rheumatoid arthritis (RA), even for those with low exposure rates of 1–10 pack years. Current smoking is also associated with severity of disease and poorer response to treatments. It is however not known whether any exposure to cigarettes impacts disease expression, especially for those who have discontinued smoking.
Objectives: To assess the disease severity in RA according to smoking status (ever-, past-, current-, non-smoker).
Methods: As part of a study to examine cigarette and marijuana smoking in rheumatic disease patients, consecutively attending rheumatology patients completed an anonymous self-administered questionnaire including: pain severity on visual analog scale (VAS), patient global assessment (PtGA) and cigarette or marijuana smoking status. Concomitant physician recorded information included: sociodemographics, co-morbidities, treatments for RA, physician global assessment (PGA). Patients were categorized according to smoking status. Categorical variables were compared between groups with the Chi-Square test and continuous variables with the Student's t-test. Variables showing a statistical trend ($p<0.15$) in univariate analysis were considered in multivariate logistic regression.