in persons with RA found that 31% of their 115 person sample was cognitively impaired and stated that further studies should be done to identify the specific domains of cognitive function that are most commonly affected (1). In this project, I will be looking at and summarizing all the data and findings that have been collected and reported on CF in the RA population and seeing which domains of cognition differ and which do not differ when compared to the general population and aged based population norms.

Objectives: To conduct a systematic review of studies reporting on cognitive function (CF) in rheumatoid arthritis (RA) patients compared to non-RA populations (based on comparison with a control group or age-based population norms).

Methods: We conducted a comprehensive literature search of MEDLINE, EMBASE, and PUBMED databases using the following search terms: rheumatoid arthritis or arthritis or inflammatory arthritis, and cognitive function or cognition. The search was conducted with no limit for years, and confined to only articles in English or French. After title and abstract screen, relevant articles were selected for review. Only full length articles were considered. Study selection criteria included: 1) must be presenting original data, 2) must contain RA group with confirmed diagnosis, 3) must be reporting on CF in RA, 4) must use a validated measure of CF (self-reported or from conducting CF tests), and 5) must contain a healthy control group or age-based populations norms. Selected articles were critically appraised using the SIGN Methodology Checklist and data extracted using a standardized form.

Results: Our initial literature search yielded 747 titles, and after screening for irrelevant titles and duplicates, 28 abstracts remained. Upon excluding non-full length articles and articles which did not report on CF, 13 abstracts remained. Of these 13 articles, 8 met our selection criteria. All studies were published after the year 2000, 3 were from the USA, 1 from Canada, 1 from the UK, 1 from Australia, 1 from Egypt, and 1 from Taiwan. Sample sizes for RA and control groups varied from 15 to 120. Of these 8 articles, 6 found a significant difference in cognitive function in the RA group compared to control group or age-based population norms in at least one domain of CF. All articles that found a significant difference in CF used standardized neuropsychological tests. Domains of CF that differed included fluency, attention, visual-spatial learning, memory, decision making time, and simple reaction time. Domains of CF that were not found to differ from general population across all studies included reasoning, comprehension, and intelligence (IQ).

Conclusion: Overall, 75% of the articles reviewed found a significant difference in at least one domain of CF in RA patients compared to healthy controls or age-based population norms. The domains of CF most commonly affected are those related to processing and speed rather than intellectual ability. Further studies are needed to explore these differences in greater depth and to understand the underlying reasons for these differences.

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AB0283

IDENTIFICATION OF NEW AUTOANTIBODIES FOR RHEUMATOID ARTHRITIS USING HUMAN PROTEOME MICROARRAYS

LI Lin¹, Jinhui Tao², Hong-Liang Zhang³, Yu-Jie Tang³, LI Xin-Ya³, Qun-Qun Lu¹, Ya-Ling Wang¹, Zi-Wen Zhu¹. ¹Anhui Medical University Affiliated Provincial Hospital, Hefei, China; ²The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China; ³Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China

Background: Rheumatoid arthritis is an autoimmune disease characterized by symmetrical small arthritis. Anti-cyclic citrullinated peptide antibodies and rheumatoid factor are commonly used to diagnose RA^[1]. However, the early diagnosis of RA is sometimes difficult, due to the heterogeneity and negative anti-CCP antibody or RF in some patients. Therefore, it is urgent to find autoantibodies with high sensitivity and specificity as diagnostic markers for RA.

Objectives: To screen autoantibodies of RA with high sensitivity and specificity using human proteome microarrays^[2].

Methods: Firstly, a case-control method was used to analyze the serum antibodies of RA patients using human proteome microarray which composed of 20,000 proteins, and identified RA-related antibodies. Then, expanded the sample size and analyzed the expression of these candidates between RA patients and healthy controls.

Results: The serum of five RA patients and five healthy controls were selected to detect the RA-related autoantibodies by microarray, and 25 candidates were screened. Then the IgG and IgM RA-focused microarrays composed of the 25 proteins were screened with additional cohorts of 72 RA patients and 106 healthy controls. The results of IgG protein microarray showed: (1) Expression of these 25 autoantibodies in RA patients was significantly higher than those in healthy controls ($P<0.05$). (2) There was no differentially expressed protein between anti-CCP antibody and RF-negative RA patients ($n=18$) and anti-CCP antibody and/or RF-positive RA patients ($n=54$) ($P>0.05$). (3) ROC analysis showed that the combination of anti-RBPJ, anti-SH3BGR and anti-PAFAH1B3 autoantibody can be highly RA-specific biomarkers, with 66.7% sensitivity and 74.2% specificity, and the area under the curve is 0.734; meanwhile the sensitivity and specificity of the anti-CCP antibody and RF-negative RA patients diagnosis were 77.8% and 65.6%, and the area under the curve was 0.720. The results of IgM protein microarray showed: (1) Only 10 out of the 25 candidates' expression was significantly higher in RA patients than healthy controls ($P<0.05$). (2) Compared with anti-CCP antibody and/or RF-positive patients, the expression of anti-PAFAH1B3, anti-RBPJ, anti-SH3BGR, anti-UBA5, anti-ANP32A, anti-PAGE2, anti-SHFM1 and anti-PDE1B was found significantly higher in anti-CCP and RF-negative patients ($P<0.05$). (3) ROC analysis showed that anti-PAFAH1B3 antibody was identified to diagnose RA with 76.2% sensitivity and 72.9% specificity, and the area under the curve was 0.768; however, there were no significance for the diagnosis of anti-CCP antibody and RF-negative RA patients ($P=0.160$).

Conclusion: The combination of IgG-type antibodies anti-RBPJ, anti-SH3BGR and anti-PAFAH1B3, the IgM-type antibody anti-PAFAH1B3 as well, has high sensitivity and specificity for the diagnosis of RA; especially the IgG-type autoantibody combination has great value for the diagnosis of anti-CCP and RF-negative RA patients.

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AB0284

HEMATOLOGICAL MARKERS OF SYSTEMIC INFLAMMATION CORRELATE WITH CLINICAL, LABORATORY AND ULTRASOUND DISEASE ACTIVITY PARAMETERS IN RHEUMATOID ARTHRITIS PATIENTS

Bożena Targonska-Stepniak, Robert Zwołak, Mariusz Piotrowski, Maria Majdan. Medical University of Lublin, Department of Rheumatology and Connective Tissue Diseases, Lublin, Poland

Background: An accurate measurement of disease activity and inflammation is essential for customizing the most appropriate management and treatment strategy in patient with rheumatoid arthritis (RA). Current data suggest that hematological markers of systemic inflammation [peripheral blood neutrophil-to-lymphocyte (NLR), platelet-to-lymphocyte (PLR) and monocyte-to-lymphocyte (MLR) ratios] could be used as novel, sensitive measures of inflammatory response, additionally to conventional laboratory and clinical markers [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Disease Activity Score of 28 joints (DAS28), tender joint count (TJC), swollen joint count (SJC)]. The ultrasonography (US) of joints enables the disease activity assessment by quantifying thickening and vascularity of the synovium.

Objectives: The goal of the study was to assess the relationship of NLR, PLR, MLR with the conventional disease activity markers (ESR, CRP, DAS28, TJC, SJC) and results of joints US, in patients with RA.

Methods: The study was conducted in the consecutive 72 patients with RA (60 women, 12 men), with the mean (SD) age 53.4 (8.9) and disease duration 16.8 (10.3) years. The following procedures were assessed for all patients: joint counts, DAS28, complete blood cell counts, ESR, CRP, US of 24 small joints.

Results: The mean (SD) values of hematological markers were as follows: NLR 3.24 (2.7) (range 0.2-13.96); PLR 193.26 (88.3) (range 71.2-560.8); MLR 0.3 (0.16) (range 0.06-0.87). The mean values of NLR and PLR were significantly lower in patients with low (DAS28 $\leq$ 3.2) vs moderate/high (DAS28 $>$ 3.2) disease activity; respectively NLR 2.4 (1.7) vs 4.0 (3.2), $p=0.004$; PLR 168.7 (58.0) vs 215.8 (104.9), $p=0.4$. Hematological markers of systemic inflammation were significantly, positively correlated with clinical, laboratory and US markers of the disease activity. Significant correlations were found between: NLR and DAS28, TJC, SJC, ESR, CRP, vascularity of synovium in US; PLR and DAS28, TJC, SJC, ESR, CRP, vascularity and hypertrophy of synovium in US; MLR and DAS28, SJC, ESR, CRP, vascularity and hypertrophy of synovium in US. In multiple regression test significant correlations were confirmed for: NLR and SJC ($p=0.008$), ESR ($p<0.001$), CRP ($p<0.01$), vascularity of synovium in US ($p=0.02$); PLR and ESR ($p=0.03$), CRP ($p=0.03$); MLR and DAS28 ($p=0.04$), ESR ($p<0.001$), hypertrophy of synovium in US ($p=0.02$).

Conclusion: The results of the study suggest that hematological markers of systemic inflammation (NLR, PLR, MLR) may serve as reliable, inexpensive and effective measure of inflammation in RA. The strong association with US imaging is an attractive result because of its predictive value and usefulness in clinical practice

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AB0285

PREDICTORS OF UNACCEPTABLE PAIN, AND UNACCEPTABLE PAIN WITH LOW INFLAMMATION, IN EARLY RHEUMATOID ARTHRITIS

Anna Eberhard¹, Tor Olofsson^{2,3}, Lennart T.H. Jacobsson⁴, Carl Turesson^{1,3}.

¹Lund University, Rheumatology, Department of Clinical Sciences, Malmö, Malmö, Sweden; ²Lund University, Rheumatology, Department of Clinical Sciences, Lund, Lund, Sweden; ³Skåne University Hospital, Department of Rheumatology, Malmö, Sweden; ⁴Sahlgrenska Academy at Gothenburg University, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden

Background: Pain is a major symptom in many patients with rheumatoid arthritis (RA). In early RA, pain is usually due to active synovitis, but over the disease course some patients experience pain without elevated laboratory markers of inflammation.

Objectives: To investigate predictors of unacceptable pain, and unacceptable pain with low inflammation, in patients with early RA.

Methods: Consecutive patients with early RA (symptom duration $<$ 12 months), recruited in 1995-2005 from a defined area, were followed through 5 years. Patients were managed according to usual care, with no pre-specified treatment protocol. Pain was assessed using a visual analogue scale (VAS; 0-100 mm). Unacceptable pain was defined as VAS pain $>$ 40 based on the patient acceptable symptom state (PASS) (1), and low inflammation as CRP $<$ 10 mg/l (2). Baseline predictors of unacceptable pain, and of unacceptable pain with low inflammation, were evaluated using logistic regression analysis.

Results: A total of 233 patients with early RA (73% female, 57% anti-CCP positive, mean age 60 years, median symptom duration 7 months) were included. Of these, 179 attended the 5-year follow-up. At 5 years, 34% had unacceptable pain, and 23% had unacceptable pain with low inflammation. High VAS scores for pain and patient's global assessment (PGA) at baseline were associated with unacceptable pain at 5 years (Table). There was a negative association between baseline swollen joint count (SJC28) and unacceptable pain at the 5 year follow-up. In multivariate logistic regression analysis including VAS PGA and SJC28, both had an impact on unacceptable pain after 5 years (adjusted odds ratios per standard deviation (SD), with 95% CI 1.78 (1.26-2.52) and 0.61 (0.42-0.89), respectively). Anti-CCP positive patients were significantly less likely to experience unacceptable pain with low inflammation at 5 years (Table).

Table 1.

Baseline predictors of unacceptable pain or unacceptable pain with low inflammation in the early RA cohort after 5 years, bivariate logistic regression

Variable	Unacceptable pain		Unacceptable pain with low inflammation	
	Odds ratio	95 % CI	Odds ratio	95 % CI
Female	1.24	0.62 – 2.47	1.87	0.80 – 4.40
RF positive	0.88	0.46 – 1.67	0.54	0.26 – 1.09
Anti-CCP positive	0.77	0.39 – 1.49	0.50	0.22 – 0.98
Erosion	0.62	0.26 – 1.49	0.62	0.22 – 1.72
Age	1.09	0.80 – 1.49	0.97	0.68 – 1.38
Symptom duration	1.28	0.93 – 1.76	1.19	0.83 – 1.71
VAS pain	1.40	1.02 – 1.91	1.34	0.94 – 1.92
DAS28	1.03	0.76 – 1.41	1.00	0.70 – 1.42
SJC28	0.71	0.51 – 0.99	0.70	0.47 – 1.03
TJC28	0.98	0.71 – 1.35	1.04	0.72 – 1.50
HAQ	1.01	0.74 – 1.37	1.01	0.72 – 1.43
CRP $>$ 9 mg/l	0.64	0.29 – 1.41	0.62	0.23 – 1.72
ESR	0.79	0.57 – 1.09	0.74	0.50 – 1.11
VAS PGA	1.60	1.16 – 2.21	1.39	0.98 – 2.00

Odds ratios per SD for continuous variables

Conclusion: More than 1/3 of early RA patients experienced unacceptable pain after 5 years. Extensive synovitis in early RA was associated with a reduced risk of unacceptable pain at 5 years, likely due to positive effects of treatment on inflammation related pain. Non-inflammatory pain may be a greater long term problem in anti-CCP negative patients.

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AB0286

STATINS TO PREVENT RHEUMATOID ARTHRITIS (STAPRA TRIAL): CHALLENGES IN RECRUITMENT AND RETENTION

Laurette van Boheemen¹, S.A. Turk¹, van Beers - Tas¹, W.H. Bos², E.N. Griep³, A. M. van Sijl⁴, Maarten Boers⁴, Michael Nurmohamed⁴, Dirkjan van Schaardenburg⁵.
¹ARC Reade, Amsterdam, Netherlands; ²Sint Maartenskliniek, Nijmegen, Netherlands; ³Antonius Ziekenhuis, Sneek, Netherlands; ⁴ARC VUmc, Amsterdam, Netherlands; ⁵ARC AMC, Amsterdam, Netherlands

Background: Primary prevention may be possible in subjects at high risk to develop rheumatoid arthritis (RA). We designed a placebo controlled randomized trial to investigate if atorvastatin can halt RA development in persons at risk for this disease (STAPRA, Netherlands Trial Register NTR5265). A statin was chosen because these drugs reduce disease activity in RA (1), hyperlipidemia patients on statins have a lower risk for developing RA (2) and dyslipidemia increased the risk for RA in a sero-positive arthralgia cohort (3). We assumed that high risk-subjects would be attracted to this trial. However, we experienced severe difficulties with patient inclusion and treatment adherence.

Objectives: To explore difficulties with patient recruitment and retention.

Methods: The STAPRA study is a multicenter, 3-year, randomized, placebo controlled, double-blind clinical trial to assess the efficacy of atorvastatin 40 mg daily in delaying or preventing RA development in persons at high risk, defined by the presence of arthralgia and the presence of high titers of anti-citrullinated protein antibody (ACPA) or presence of both ACPA and rheumatoid factor (RF). Eligible participants were $\geq$ 18 years, did not use lipid lowering agents and had no synovitis. Five centers participated. Our goal was to recruit 220 study subjects based on an expected risk reduction of 21%. The unexpected low recruitment rate prompted us to evaluate the reasons to decline participation or to discontinue the study drug prematurely.

Results: Details were available from the initiating center (Reade) and 1 participating center (Sint Maartenskliniek (SMK)). During a period of 36 months, 164 eligible patients were asked to participate of whom 58 patients (35%) consented. Most common reasons to decline were: unwillingness to use study medication (49%) and the feeling that participation was too time-consuming (14%). Fifty-four patients were randomized since 4 failed screening due to hyperlipidemia or seronegativity on repeated testing. Currently, 11 participants (20%) have developed arthritis. Twelve