Methods: We evaluated 316 patients with established RA from a single center. Beliefs about the necessity of RA medications and concerns regarding their use were evaluated with the Beliefs about Medicines Questionnaire-Specific (BMQ) Necessity and Concerns scales (range 5-25). Self-reported rheumatoid arthritis treatment adherence was assessed using the Simplified Medication Adherence Questionnaire (SMAQ, range 0-6). Multivariable linear regression evaluated the effects of necessity, concerns and their interactions with adherence. A latent profile analysis (LPA) subsequently reclassified patients in groups according to patterns of necessity and concerns; adherence scores were then compared across latent groups using ANCOVA.

Results: Full adherence (SMAQ score 6/6) was reported by 101 (32%) patients. Necessity and concerns had independent and opposing contributions to adherence ($\beta=0.21$ and $\beta=-0.28$ respectively, $p<0.001$ and figure 1a) even after adjustments for age, gender and disease duration. An interaction between necessity and concerns with adherence was also observed ($p=0.009$); post-hoc simple-slope tests showed that necessity predicted adherence with increasing concerns. Johnson-Neyman technique revealed that while concerns were significantly associated with adherence across the entire range of necessity scores, necessity was significantly related to adherence only at BMQ Concerns scores ≥ 13 . LPA revealed four latent patient groups: Low necessity/Low concerns (indifferent, $n=33$), Low necessity/High concerns (skeptical, $n=70$), High necessity/High concerns (ambivalent, $n=92$) and High necessity/Low concerns (accepting, $n=121$). Adherence varied across groups even after adjusting for between-group differences ($p=0.002$, Figure 1b); adherence was highest in the accepting group and lowest in the skeptical group.

Conclusion: The relationship between necessity and concern beliefs regarding RA medications significantly influences adherence behavior and may further direct physicians to effectively target their education efforts. A message aimed at reducing concerns might be more effective in the ambivalent subgroup, whereas emphasizing medication necessity may be more fruitful in the skeptical group.

Figure 1. Interaction between Necessity and concerns on medication adherence in RA

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SAT0096

CORRELATION OF GROWTH FACTORS WITH RHEUMATOID ARTHRITIS CLINICAL COURSE INDICATORS

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Background: The evaluation of early destruction markers in rheumatoid arthritis (RA) is of significant clinical importance for improving the patient's life quality. One of the immunological markers of RA early diagnosis and of severe disease is antibodies to cyclic citrullinated peptide (ACCP). Instrumental methods for early diagnosis of RA include the ultrasound of joints. Vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF) can stimulate the processes of angiogenesis and proliferation, which in turn can increase the infiltration and hyperplasia of synovia, the growth of pannus mass and contribute to the development of bone and cartilage erosions.

Objectives: to establish the correlation of growth factor indicators with markers of the destructive course of rheumatoid arthritis.

Methods: 194 patients with a diagnosis of RA were examined, among the examined patients women prevailed - 86.6%, the age was 47.7 ± 10.22 years. Positive by the presence of ACCP (> 20 U/ml) was 76.8%, and negative - 23.2%. The ELISA in the serum was determined by the concentration of CRP and TNF- α (Vector-Best, Russia), antibodies to cyclic citrullinated peptide (ACCP) (Euroimmun, Germany), VEGF and FGF (BCM Diagnostic, Canada). Ultrasound of the joints was performed by the device "ESAOTE MyLAB40" (Netherlands, 2011) with a linear sensor of 7.5 L 70 (frequency 7.5 MHz), semi-quantitative evaluation of indicators was used: effusion into the joint space (JS), synovial thickness, vascularization of the synovial membrane (SM), the presence of pannus and bone-cartilage erosion.

Results: Direct correlations with CRP and ACCP levels ($p = 0.02$; $p = 0.01$, respectively), TNF α and DAS28 ($p < 0.001$) were established during analysis of the correlation links between VEGF and RA clinical course indicators. Analysis of the correlation of VEGF and ultrasound indices of the joints in the examined patients RA established strong direct links with the JS effusion parameters and the SM vascularization assessment ($p < 0.001$, in all cases), and a direct interaction of weak force with the indicator of pannus ($p = 0.04$) was found. Regression analysis of the dependence of the variability of the SM vascularization assessment on the level of VEGF in the blood showed a sufficient value of the coefficient of determination (0.57), and the data of the normalized index DW = 2.09 reliably indicate the absence of autocorrelation (0.06).

Direct correlations with R $\ddot{o}$ stage ($p < 0.001$) and the rate of CRP ($p = 0.02$) were established during analysis of correlation links of FGF with the RA clinical course. Analysis of the correlation of FGF and ultrasound indices of the joints in the examined RA patients established strong direct correlations with the indicators of the thickness of SM, pannus, and bone-cartilage erosion ($p < 0.001$, in all cases), the direct correlation of weak force ($p = 0.04$) was with the SM vascularization assessment index. Regression analysis of the dependence of the variability of the SM thickness indicator on the FGF blood level showed a sufficient value of the multiple correlation $R^2 = 0.47$. Also showed a regression analysis of the dependence of the variability of pannus and bone and cartilage erosion indices on the FGF blood level ($R^2 = 0.51$; $R^2 = 0.46$, respectively), which evidences the regression line approximation to the observed data.

Conclusion: According to the correlations of VEGF, FGF levels with CRP, ACCP, assessment of synovial vascularization and bone-cartilage erosions - the high levels of VEGF, FGF in the blood can be used as markers of severe destructive course of RA and of the high rate of disease progression, which requires the early aggressive basic therapy of RA with the use of genetically engineered biologic drugs prescription.

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SAT0097

ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND SUBSEQUENT CHANGES IN DISEASE ACTIVITY IN PEOPLE LIVING WITH RHEUMATOID ARTHRITIS

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Background: Various studies have found that rheumatoid arthritis (RA) patients perform less physical activity than the general population, likely due to joint pain and impaired physical function. However, recent studies suggest that physical activity may have a beneficial effect on inflammation and could therefore contribute to reducing RA disease activity. A greater understanding of the relationship between physical activity levels and RA disease activity would be valuable for physical activity counselling of RA patients.

Objectives: The aim of this study was to evaluate the association between baseline physical activity levels and subsequent changes in measures of disease activity in patients with RA using self-reported data.

Methods: We conducted a longitudinal study using 2015-2017 data from an annual survey administered to an RA cohort derived from a population-based cohort for BC originally assembled using physician billing data and a previously validated algorithm. Subjects were grouped into three levels (Low, Medium and High) of physical activity (PA) at the baseline year (2015) according to the specifications of the International Physical Activity Questionnaire. We examined whether physical activity at baseline was associated with a change over time in RA disease activity outcomes

from 2015 to 2017. We fitted linear mixed models for Rheumatoid Arthritis Disease Activity Index (RADAI), Fatigue visual analog scale (VAS), and Pain VAS scores separately without/with adjusting for age, sex, sociodemographic factors, body mass index, RA duration, physical function (Modified Health Assessment Questionnaire [mHAQ]), smoking, depression and other comorbidities at baseline. Models include the outcome at three years (2015-2017) as the dependent variables, an indicator variable representing the year of measurement (2015-17), PA level at baseline, their interactions, and baseline characteristics as covariates. Models include random effects for subjects to account for correlations among within-subject repeated measures. Missing values were imputed using multiple imputation methods. The analyses were conducted using R 3.5.

Results: Of the 169 patients who responded to the 2015 survey, 29.6%, 42.0%, and 28.4% had low, medium, and high levels of PA in 2015, respectively. There were no significant differences in RADAI ($p=0.67$), Fatigue ($p=0.78$), and Pain ($p=0.98$) at baseline (Figure 1). The low PA group experienced significant worsening of disease activity outcomes over time, including yearly increases of 0.31 in RADAI ($p=0.007$), 0.41 in Fatigue ($p=0.007$), and 0.43 in Pain ($p=0.007$). Those in the medium and high PA groups at baseline experienced either a decrease or no change in their disease activity outcomes over time. The interaction terms for PA level and year show that the low PA group had significantly different time trends for RADAI, Fatigue, and Pain compared to the medium and high PA groups (all p values <0.05). The results remain robust after adjusting for age, sex, and other covariates.

Figure 1. Time Trends for Mean RADAI, Fatigue, and Pain by Baseline Physical Activity Level

Table 1. Linear Mixed Model without/with Adjusting for Baseline Characteristics

Model Covariates	RADAI		Fatigue		Pain	
	Coef. [95% CI]	p	Coef. [95% CI]	p	Coef. [95% CI]	p
A. Unadjusted Linear Mixed Model						
Physical Activity (PA)						
Low	ref		ref		ref	
Medium	-0.24 [-0.99, 0.52]	0.542	-0.24 [-1.26, 0.77]	0.638	0.08 [-0.87, 1.04]	0.865
High	-0.39 [-1.22, 0.44]	0.357	-0.33 [-1.44, 0.78]	0.558	-0.13 [-1.17, 0.92]	0.811
Year (Low PA Group)	0.31 [0.07, 0.54]	0.012	0.41 [0.1, 0.72]	0.009	0.43 [0.11, 0.75]	0.009
Physical Activity*Year						
Medium*Year	-0.36 [-0.67, -0.05]	0.025	-0.44 [-0.84, -0.03]	0.036	-0.5 [-0.92, -0.08]	0.021
High*Year	-0.35 [-0.69, -0.01]	0.048	-0.68 [-1.12, -0.24]	0.003	-0.54 [-1.01, -0.08]	0.021
B. Adjusted Linear Mixed Model						
Physical Activity (PA)						
Low	ref		ref		ref	
Medium	0.54 [-0.22, 1.29]	0.162	0.25 [-0.55, 1.06]	0.537	0.54 [-0.22, 1.29]	0.162
High	0.94 [0.11, 1.77]	0.027	0.74 [-0.15, 1.63]	0.105	0.94 [0.11, 1.77]	0.027
Year (Low PA Group)	0.44 [0.12, 0.77]	0.007	0.43 [0.12, 0.74]	0.007	0.44 [0.12, 0.77]	0.007
Physical Activity*Year						
Medium*Year	-0.51 [-0.94, -0.08]	0.019	-0.46 [-0.86, -0.05]	0.028	-0.51 [-0.94, -0.08]	0.019
High*Year	-0.56 [-1.03, -0.1]	0.017	-0.7 [-1.14, -0.26]	0.002	-0.56 [-1.03, -0.1]	0.017

* The difference in trends for RA disease activity outcomes between the Medium and Low PA groups.
** The difference in trends for RA disease activity outcomes between High and Low PA groups.

Conclusion: Across RADAI, Fatigue VAS, and Pain VAS scores, RA patients with a low PA level demonstrated a significant increase in disease activity over the span of three years. The trends for both the high and medium PA groups differ significantly from that of the low PA group, showing small, overall decreases in disease activity over time. These results add to the accumulating evidence that physical activity may reduce disease activity and is an essential aspect of RA management.

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SAT0098 ANTIBODIES AGAINST CITRULLINATED ANTIGENS ARE ASSOCIATED WITH TREATMENT RESPONSE IN ACPA-NEGATIVE RHEUMATOID ARTHRITIS PATIENTS

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Background: RA patients who are ACPA-positive (ACPA+) are known to have worse prognosis. Less is known regarding predictors of treatment outcomes in ACPA-negative (ACPA-) patients.

Objectives: We investigated whether autoantibodies captured on a custom array were associated with response to therapy in ACPA- RA patients.

Methods: RA patients were recruited to either the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS, starting adalimumab, established disease) or the RA Medication Study (RAMS, starting methotrexate, early disease). Serum samples were collected at pre-treatment and 3/6 months in BRAGGSS/RAMS, respectively. Treatment groups were pooled for analysis. ACPA was measured using a commercially available ELISA (Axis-Shield Diagnostics Ltd, Dundee, UK). Pre-treatment RA and healthy blood donor control (HC) serum samples were incubated on a bead-based assay (Luminex FlexMap 3D) containing 376 human protein antigens associated with autoimmune disease (39 in citrullinated (cit) form) to detect autoantibodies. Median fluorescence intensity (MFI) values were calculated for each autoantibody for RA and HC, then normalised and log2-transformed. The 95th percentile for each autoantibody in HC was used to determine whether an RA sample was positive/negative for that autoantibody. Proteins with $<10\%$ frequency in RA patients were excluded from analysis. Linear regression was used to determine autoantibodies differing in MFI between RA and HC; p -values were adjusted using the Benjamini-Hochberg correction. Significant autoantibodies (adjusted $p<0.05$) were tested for associations with treatment outcomes in RA patients only using: (i) linear regression for improvement in DAS28; (ii) logistic regression for good/poor vs all EULAR response. All regression was adjusted for age, gender, disease duration and baseline DAS28. Subanalysis was carried out in a subset of ACPA+ patients.

Results: 168 patients with RA were included in analysis (mean age 59.6 years, mean disease duration 14.3 years, 126 (75%) female patients, 90 (53.6%) ACPA+ patients). 34 autoantibodies were differentially expressed in RA patients, only one of which (TNF ligand superfamily member 13, TNFSF13) was lower than in HC. 29/34 autoantigens were in cit-form. In multivariate models of all differentially expressed autoantibodies, heterogeneous nuclear ribonucleoprotein A1 (HNRNPA1) was significantly associated with EULAR response (coefficient (coef) 0.7, 95% CI 0.1-1.3), and cit-vimentin (VIM) was significantly associated with poor EULAR response (OR_{adj} 4.2, 95% CI 1.1-18.3) and reduced odds of good EULAR response (OR_{adj} 0.2, 95% CI 0.1-0.8). ACPA remained the best predictor of treatment response. In a subanalysis of the 78 ACPA patients, cit-cleavage and polyadenylation specificity factor subunit 6 (CPSF6) was significantly associated with worse DAS28 (coef (-1.8), 95% CI (-3.6)-(-0.1)). cit-DnaJ homolog subfamily B member 1 (DNAJB1) was significantly associated with DAS28 improvement (coef 2.2, 95% CI 0.6-3.8). No autoantibody was associated with EULAR response.

Conclusion: A subset of ACPA patients have ACPA fine specificities not seen by a commercial assay. Larger ACPA profiling may provide additional information on treatment response. This requires validation with larger sample sizes and replication in an independent cohort.

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