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Background: Rheumatoid Arthritis (RA) is often associated with autonomic dysfunction, which is presumably playing a role in the pathogenesis of the disease and may contribute to disease activity [1,2]. Accordingly, patients with RA show reduced heart rate variability (HRV) [3].
Objectives: The aim of this prospective pilot study was to examine a possible connection between disease activity and activity of the autonomic nerve system in patients with RA.
Methods: In the non-randomized prospective exploratory study, patients with active RA and an upcoming change in treatment were included. Assessments were performed at baseline before treatment initiation (T0) and after 3 months (T1), including the Disease Activity Score 28 (DAS28-CRP), HRV measurement, and the physician and patient global assessment (PGA, PtGA). HRV was measured through a 5-minute ECG with finger electrodes, using Kardia App®. Total variability was measured by the variance of RR intervals over the temporal segment (Total Power) as well as by standard deviation of the average RR intervals (SDRR). Root Mean Square of successive differences (RMSSD) and percentage of number of pairs of adjacent RR intervals differing by more than 50 milliseconds (pRR50) were used for estimating parasympathetic activity. In addition, blood concentrations of Neuropeptide Y (NPY), vasoactive intestinal peptide (VIP) were measured as surrogate parameters for activity of the sympathetic (NPY) and parasympathetic (VIP) nervous system. Statistical analysis was performed using linear regression analysis.
Results: A total of 40 patients was included. Our results showed an overall improvement in both disease activity measured by DAS28-CRP (p= <0,001; SMD= 1.393) and HRV (Total Power p= 0.014; SDRR p= 0.0023) between visits (Table 1). DAS28-CRP was inversely associated with parasympathetic activity (pRR50, p= 0.0494). PtGA also correlated inversely with pRR50 (p= 0.0049). RMSSD as another parasympathetic indicator was negatively predictive for percentage change of PGA (p= 0.0109). Patients with lower parasympathetic activity at baseline had a higher change in disease activity than patients with higher parasympathetic activity at baseline.

Table 1. HRV parameters and disease activity at T0 and T1 (*all parameters at T0 and T1as mean values*)

Parameter	T0	T1	p-Wert	SMD
SDRR (ms)	36,23	64,06	0,007	0,621
RMSSD	37,61	76,64	0,013	0,565
PtGA	6,55	4,47	0,001	0,780
PGA	5,42	3,02	< 0,001	1,064
DAS28	4,25	2,76	< 0,001	1,393
SDAI	26,95	13,70	< 0,001	1,216
Remission (n)	0	16	< 0,001	1,376

DAS28 disease activity score 28, HRV heart rate variability, ms milliseconds, PGA physician global assessment, PtGA patient global assessment, RMSSD Mean Square of successive differences, SDAI Simple Disease Activity Index, SDRR standard deviation of the average RR intervals, SMD standardized mean difference

Conclusion: The results of our prospective study underline the importance of the autonomic nerve system regarding disease activity and prognosis in RA. Higher parasympathetic activity was associated with lower disease activity. Patients with initially lower parasympathetic profile and higher disease activity benefited to a greater extend from initiation or change of therapy. In our study, the specific blood parameters NPY and VIP showed no relevant association with disease activity and treatment response.
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AB0198

THRESHOLDS OF PRESENTEEISM MEASUREMENT INSTRUMENTS FOR UNACCEPTABLE WORK PARTICIPATION AND FUTURE ADVERSE WORK OUTCOMES IN RA

Keywords: Rheumatoid arthritis, Patient reported outcomes, Work-related issues

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Background: Presenteeism is associated with lower work satisfaction and increased risk of future sick leave in rheumatic diseases. Presenteeism is generally measured on a continuous scale; however, despite a lower precision, identifying persons with a meaningful level of presenteeism can improve interpretation in clinical studies and might be useful in routine practice. Recently, thresholds of meaning for presenteeism instruments were established for axial spondyloarthritis (axSpA).
OBJECTIVES:
1)To identify thresholds for presenteeism instruments that reflect unacceptable work status in patients with RA and whether those thresholds could predict future adverse work outcomes (AWO);
2)To assess in patients with RA the performance of presenteeism thresholds previously established in axSpA for the same instruments.
Methods: We used data from the 1-year multinational prospective study on Patient-Reported Outcomes in Employment Study in Rheumatoid Arthritis (RA-PROSE). Thresholds to determine when patients consider themselves in 'unacceptable work status' were calculated at baseline for 4 presenteeism instruments (Work Productivity and Activity Impairment questionnaire -WPAI-, Quality and Quantity method -QQ-, Workplace Activity Limitations Scale -WALS- and Work Limitations Questionnaire -WLQ 25-) and for a patient global assessment of pain. We created receiver operating characteristic (ROC) using as external criterion a Patient Acceptable Work State question, addressing one's ability to perform their current job satisfactorily. We used different approaches (75th percentile, Youden index, Liu method, nearest to 0.1) to determine the optimal cut-off, while balancing over-under diagnosis. Accuracy of thresholds to predict "future adverse work outcome" throughout 12 months (defined as sick leave or long-term disability) was assessed. The recently developed presenteeism thresholds for axSpA were also tested.
Results: A total of 105 employed patients were included: 77% females, mean age 48 (SD 9), with a mean symptom duration of 9.8 (8.7) years. 15% of the patients considered themselves in an unacceptable work status and 7 (8%) had at least one AWO during 12 months. All instruments (presenteeism and pain) showed good performance vs the external criterion (AUC >0.75) except for the QQ method (AUC 0.62). The Table 1 shows the optimal thresholds for each instrument and their performance to correctly identify an unacceptable work status and AWO during 12 months for the RA-specific threshold (1st row) and the available axSpA threshold (2nd row). Interestingly, the axSpA thresholds performed better to classify work status as 'unacceptable' and to predict AWO. For adverse work outcome over 12 months, pain and WPAI performed better specially in predicting AWO.
Conclusion: Thresholds for presenteeism and pain representing unacceptable work status have been established for RA. Previously developed thresholds for axSpA showed an even better performance and are therefore the preferred to be used. WPAI performed the best and can be used to identify patients requiring more tailored care in order to avoid future AWO.

Table 1. Optimal thresholds for presenteeism measures and patients correctly classified for unacceptable work status and adverse work outcome during 12 months.

	Optimal threshold (SE/SP)	Correctly classified for unacceptable work status n (%)	Correctly classified for AWO during 12 months n (%)
WPAI presenteeism (0-100)	**≥30 (89/70)**	66 (73)	57 (69)
	≥40 (78/82)	77 (82)	62 (75)
QQ method (0-10)	**≥2 (67/55)**	53 (56)	49 (59)
	≥3 (56/64)	59 (63)	57 (69)
WALS (0-3)	**≥0.61 (89/59)**	51 (62)	44 (61)
	≥0.75 (67/68)	56 (68)	49 (68)
WLQ 25 (0-100)	**≥27 (89/77)**	53 (57)	45 (55)
	≥29 (77/80)	57 (61)	46 (56)
Pain (0-10)	**≥4 (67/68)**	64 (68)	61 (73)

The final thresholds are colored in green and correspond to the one's derived from axSpA. For pain measurement there was no axSpA derived threshold.

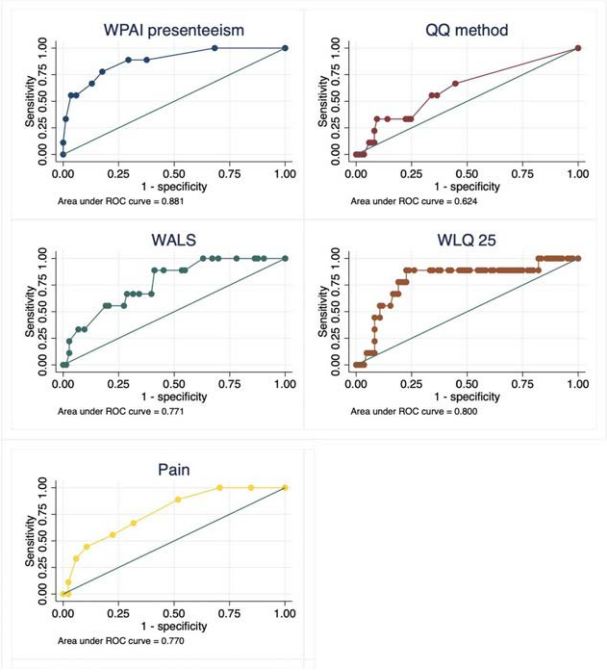

Figure 1. ROC curves for presenteeism (4 different measurement instruments) and for pain according to unacceptable work status

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AB0199

THE PROGNOSTIC VALUE OF IGA ANTI-CITRULLINATED PROTEIN ANTIBODY AND RHEUMATOID FACTOR IN AN EARLY ARTHRITIS COHORT WITH A TREAT-TO-TARGET APPROACH

Keywords: Prognostic factors, Rheumatoid arthritis, Autoantibodies

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Background: The EULAR research agenda states that new biomarkers are needed to stratify patients and to predict therapeutic response or lack of response in rheumatoid arthritis. Currently, IgG anti-citrullinated protein antibody (ACPA) and IgM rheumatoid factor (RF) are used as poor prognostic factors for treatment decisions in RA. The mucosal origin hypothesis of RA renewed the interest in the role of IgA isotype autoantibodies for disease pathogenesis. However, the value of IgA ACPA and RF for prognostication of treatment response under a treat-to-target approach is not clear to date.
Objectives: To evaluate the prognostic value of IgA ACPA and RF by considering 'quick-attained and persistent remission', DMARD-free remission (DFR) and biological use in an early (rheumatoid) arthritis population.
Methods: All patients from the treatment in the Rotterdam Early Arthritis Cohort (tREACH) trial with available baseline sera were included. The tREACH trial is a multicentre, stratified, single-blinded trial with a treat-to-target approach. IgA ACPA and RF isotypes were measured by automated fluorescence enzyme-immuno assay (FEIA) in baseline sera. The prognostic value of positivity for IgA ACPA and RF was evaluated for three outcome measures: (1) quick-attained (at 6 months) and persistent (to 2 years) remission, analysed with logistic regression analysis; (2) achievement of DFR for at least 6 months over a 2 year follow-up period, analysed with survival analysis; and (3) incident biological use over 2 years, analysed with mixed effects logistic regression analysis. Results were stratified for IgG ACPA, since it is known that IgG ACPA is related to lower (DMARD-free) remission rates and more biological use.
Results: IgA isotypes of ACPA and RF were measured in baseline sera of 480 tREACH patients. 66% was female, mean age was 53 years, median symptom duration 21 weeks, and median swollen joint count 5. A positive IgA ACPA titre was present in 109 (23%) patients and most of them also had a IgG ACPA result above the cut-off value for positivity (n=102, overlap of 94%). Positive IgA RF on the other hand was present in 172 (36%) of patients, which overlapped with IgM RF for 90% (n=154). Double positivity for IgA and IgG ACPA (n=102) revealed lower DFR rates after 2 years compared to IgG ACPA positivity alone (6% and 11%, respectively, Figure 1A), although this finding was not significant (p=0.09). No differences were observed in 'quick-attained and persistent remission' and biological use for both IgA ACPA and RF, after stratification for IgG ACPA.
Conclusion: IgA isotypes of ACPA and RF almost completely overlap with the commonly measured isotypes (IgG ACPA and IgM RF, respectively). In addition, both an IgA ACPA and IgA RF response do not predict persistent remission, DFR and biological use in this treat-to-target population. Based on these results, there is no rationale for measuring these isotypes in newly diagnosed (rheumatoid) arthritis patients in daily clinical practice.

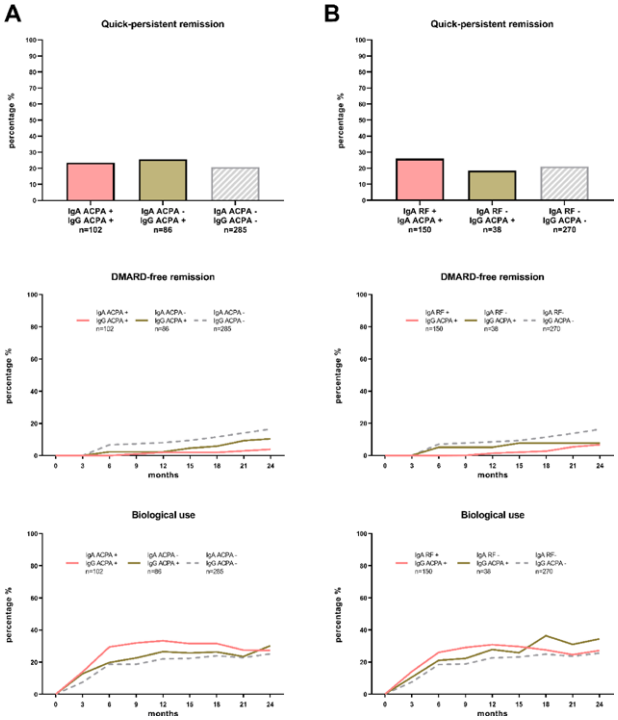

Figure 1. Quick-persistent (6-24 months) remission, DMARD-free remission and biological use over 2 years in (A) IgA/IgG ACPA positive patients vs. IgG ACPA positive patients, with IgA/IgG ACPA negative patients as a reference group; and in (B) IgA RF/IgG ACPA positive