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POS0306

IMPACT OF MULTIMORBIDITY ON DISEASE MODIFYING ANTI-RHEUMATIC DRUG THERAPY IN EARLY RHEUMATOID ARTHRITIS: DATA FROM THE ESPOIR COHORT

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Background: Multimorbidity is frequent in rheumatoid arthritis (RA) and could interfere with the therapeutic response.

Objectives: The aim of this study was to evaluate multimorbidity in the French cohort of early arthritis (ESPOIR cohort) and its possible impact on the therapeutic response.

Methods: We included patients fulfilling 2010 ACR/EULAR criteria for RA. An adapted MultiMorbidity Index (aMMI) was developed [1]. Each patient was assigned scores of binary aMMI (0= no comorbidity, 1= at least 1 comorbidity) and counted and weighted aMMI. The primary endpoint was achievement of Clinical Disease Activity Index (CDAI) low disease activity after initiation of a first disease-modifying anti-rheumatic drug (DMARD) according to the aMMI. Secondary endpoints were other disease activity scores and response criteria. We collected data from the visit preceding the first DMARD initiation (baseline visit) and the visit after at least 3 months of treatment (follow-up visit). The impact of aMMI on therapeutic maintenance at 1, 3, 5 and 10 years was evaluated.

Results: Analyses involved 472 patients: 302 (64%) had at least 1 comorbidity. Overall, 45.3% and 44.7% with binary aMMI= 0 or 1, respectively (p= 0.9), achieved CDAI low disease activity (Table 1). Similar results were found with counted and weighted aMMI. Use of other disease activity scores or response criteria did not show a significant impact of multimorbidity on the therapeutic response. Therapeutic maintenance was significantly better with binary aMMI = 1 than binary aMMI = 0. Increased counted aMMI was associated with increased probability of still being on the first initiated DMARD at each time point (Table 2).

Conclusion: In the ESPOIR cohort, therapeutic response to a first DMARD was not affected by multimorbidity but therapeutic maintenance was better in multimorbid patients.

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Table 1. Impact of aMMIs on CDAI, DAS28 and SDAI low disease activity (LDA) achievement at follow-up visit (univariate analyses)

	LDA achievement								
	CDAI			DAS28			SDAI		
	Yes	No	p	Yes	No	p	Yes	No	p
Binary aMMI, n (%)									
0	77 (45.3)	93 (54.7)	0.9 [*]	85 (50.0)	85 (50.0)	0.2 [*]	80 (47.1)	90 (52.9)	0.9 [*]
1	135 (44.7)	167 (55.3)		131 (43.4)	171 (56.6)		141 (46.7)	161 (53.3)	
Counted aMMI, mean (SD)	1.0 (1.1)	1.1 (1.1)	0.7	1.0 (1.1)	1.1 (1.1)	0.2	1.1 (1.1)	1.1 (1.1)	1.0
Weighted aMMI, mean (SD)	4.1 (5.2)	4.0 (4.7)	0.9	4.0 (5.2)	4.1 (4.7)	0.3	4.0 (5.0)	4.0 (4.9)	1.0

aMMI= adapted MultiMorbidity Index; CDAI= Clinical Disease Activity Index; SDAI= Simplified Disease Activity Index^{*} Proportion of patients achieving LDA between patients with binary aMMI= 0 and binary aMMI= 1. Because of no statistically significant results, no multivariate analysis was performed.

Table 2. Probability of first DMARD maintenance at 1, 3, 5 and 10 years (multivariate analysis)

Time point	First DMARD maintained or stopped	Binary aMMI [#]		Counted aMMI [§]
		0	1	
1 year	Maintenance (n= 300) OR [95% CI]*	2 [286.2->999]	298 > 999	1.71 (0.93) 221.3
(n= 530)	Withdrawal (n= 230)	205	25	[84.0-583.0] 0.12 (0.37)
3 years	Maintenance (n= 285) OR [95% CI]*	10 153.9	275	1.66 (0.94) 26.1
(n= 493)	Withdrawal (n= 208)	175	33	[73.0-324.5] [15.1-45.3] 0.22 (0.64)
5 years	Maintenance (n= 116) OR [95% CI]*	9 10.9	107	1.72 (1.05) 2.2
(n= 459)	Withdrawal (n= 343)	163	180	[5.1-23.3] [1.8-2.7] 0.82 (1.0)
10 years	Maintenance (n= 40) OR [95% CI]*	2 14.0	38	1.58 (0.84) 1.6
(n= 415)	Withdrawal (n= 375)	158	217	[3.3-59.1] [1.2-2.0] 0.99 (1.12)

[#]data are number of patients[§] data are mean (standard error)* data are odds ratios (ORs) and 95% confidence intervals (95% CI) of still being on the first initiated DMARD at 1, 3, 5 and 10 years between patients with binary aMMI = 1 and binary aMMI = 0 and according to counted aMMI, per additional point.

The variables included in multivariate analyses were sex, rheumatoid factor and/or anti-citrullinated peptide antibody positivity, age, CDAI at baseline visit, number of treatments at baseline visit.

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POS0307

FATIGUE IN RHEUMATOID ARTHRITIS PATIENTS IS ASSOCIATED TO SUBJECTIVE BUT NOT OBJECTIVE ASSESSMENTS OF DISEASE ACTIVITY DURING TREATMENT WITH TOCILIZUMAB

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Background: Fatigue is common in patients with rheumatoid arthritis (RA), and its association with inflammatory activity is not fully understood.

Objectives: To explore the associations between fatigue and inflammation by clinical, laboratory and ultrasound examinations during follow-up of RA patients on biological treatment.

Methods: A Nordic (Denmark, Finland, Norway, Sweden) open-label, single-arm study (part of the umbrella program – TOZURA (1)), enrolled patients with inadequate response to conventional synthetic (cs) DMARDs. Patients received tocilizumab 162mg sc weekly for 24 weeks as monotherapy or in combination with a csDMARD. Stable oral NSAIDs and corticosteroids (≤ 10 mg/day prednisone or equivalent), were allowed. Patients were assessed at baseline, 4, 12 and 24 weeks for fatigue (FACIT-F questionnaire (total sum scores)), patient reported outcome measures (PROMs) including joint pain and patient's global visual analogue scale (VAS) as well as HAQ-DI, clinical assessments (tender and swollen joints, assessor's global VAS), laboratory examinations (ESR, CRP) and ultrasound assessments (36 joints and 4 tendons, scored according to the Norwegian US atlas (2)). Spearman correlations, performed both at baseline and for changes from baseline of variables during follow-up, explored associations between fatigue and PROMs, clinical, laboratory as well as ultrasound variables. Predictive value of fatigue was investigated by linear regression.

Results: 110 patients were included (83% female, mean (SD) age 55.6 (12.1) years and RA duration 8.7 (9.5) years, 81% anti-CCP positive). All PROMs, clinical, laboratory and ultrasound variables decreased significantly, already after 4 weeks ($p < 0.001$). Both for baseline assessments as well as for changes during follow-up, fatigue was associated with PROMs (Table 1 (baseline) and Table 2 (follow-up)). However, there were no or low associations between fatigue and clinical, laboratory and ultrasound assessments at baseline or during follow-up. In addition, baseline fatigue was predictive of joint pain, patient's global VAS and HAQ-DI during follow-up ($p < 0.05$ – 0.001), but not for the clinical, laboratory or ultrasound assessments.

Conclusion: Fatigue assessed by an established questionnaire did not show any associations with several assessments of inflammatory activity in RA patients, neither at baseline nor during effective treatment. Thus, the present study adds to the increasing number of papers finding fatigue to reflect other aspects of RA disease activity than inflammation.

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Table 1. Spearman correlations between FACIT-F total score and patient reported outcomes, clinical, laboratory and ultrasound assessments. * $p < 0.05$. ** $p < 0.001$

	Baseline	4 weeks	12 weeks	24 weeks
Patient's global VAS	-0.46**	-0.41**	-0.50**	-0.48**
Joint pain VAS	-0.43**	-0.50**	-0.54**	-0.41**
HAQ-DI	-0.59**	-0.59**	-0.60**	-0.62**
28 tender joint count	-0.07	-0.19	-0.12	-0.22*
28 swollen joint count	0.14	0.12	0.20*	0.19
Examiner's global VAS	0.05	0.05	-0.03	-0.15
ESR (mm/h)	-0.02	-0.01	0.07	-0.04
CRP (mg/L)	-0.11	-0.02	0.06	0.07
Sum score GS	0.09	0.20*	0.24*	0.13
Sum score Doppler	0.06	0.01	0.13	0.02

Table 2. Spearman correlations between changes in FACIT-F total score from baseline to 4, 12 and 24 weeks and changes in patient reported outcomes, clinical, laboratory and ultrasound assessments. * $p < 0.05$. ** $p < 0.001$

	4 weeks	12 weeks	24 weeks
Patient's global VAS	-0.59**	-0.56**	-0.59**
Joint pain VAS	-0.60**	-0.50**	-0.52**
HAQ-DI	-0.43**	-0.44**	-0.61**
28 tender joint count	-0.29*	-0.30*	-0.24*
28 swollen joint count	-0.15	-0.17	-0.06
Examiner's global VAS	-0.14	-0.27*	-0.15
CRP (mg/L)	-0.19	-0.21*	-0.25*
ESR (mm/h)	-0.13	-0.18	-0.21
Sum score GS	-0.10	-0.17	-0.12
Sum score Doppler	-0.21*	-0.14	-0.10

Disclosure of Interests: Hilde Berner Hammer Speakers bureau: AbbVie, Pfizer, Roche, Lilly and Novartis, Consultant of: Novartis, Birte Aguilar Employee

of: Roche, Lene Terslev Speakers bureau: Roche, MSD, BMS, Pfizer, AbbVie, Novartis and Janssen

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POS0308 TRAJECTORIES OF FATIGUE IN EARLY RA OVER 10 YEARS: RESULTS FROM THE ESPOIR COHORT

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Background: Fatigue is one of the most prevalent symptom reported by persons with RA. RA-related fatigue is a complex concept with biological, psychological and social interactions.

Objectives: In a cohort of early RA patients, to determine and characterize fatigue trajectories over 10 years of follow-up and identify predictors of trajectory membership.

Methods: Patients fulfilling the 2010 ACR/EULAR criteria for RA included in the ESPOIR cohort. We used a cluster analysis to obtain fatigue (assessed by fatigue visual analogue scale) trajectories over the course of 10 years from enrolment. Chi-square tests or ANOVA were performed to evaluate differences of baseline variables between fatigue trajectories. Using a multinomial logistic regression we could identify predictors of trajectory membership.

Results: We analysed 598 patients with mean disease duration at enrolment of 26.2 ± 40.9 days. Cluster analysis revealed 3 trajectories: high (18%), moderate (52%) and low fatigue (30%). Compared to patients with moderate or low fatigue trajectory, patients with high fatigue trajectory were predominantly women and reported significantly higher duration and intensity of morning stiffness, HAQ score, number of tender joints, levels of pain, number of awakenings due to arthritis, levels of physician and patient global assessment and more frequent sleep problems, and increased psychological distress. Female patients with pain, psychological distress and presence of sicca symptoms had higher risk of being in high trajectory group.

Conclusion: These findings suggest that levels of fatigue are rather stable over time in each trajectory. Baseline clinical measures and baseline patient-reported measures of functional status better distinguished the three fatigue trajectories. We did not find differences between trajectories in baseline laboratory measures. Inflammatory activity was not a predictor of being in high trajectory fatigue group.

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POS0309 SEROPOSITIVITY INCREASES RISK OF INCIDENT DEMENTIA IN INDIVIDUALS WITH RHEUMATOID ARTHRITIS: A POPULATION-BASED COHORT STUDY

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