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FRI0054

CHANGES IN DEPRESSIVE SYMPTOMS IN RHEUMATOID ARTHRITIS (RA) PATIENTS DURING TOCILIZUMAB (TCZ) THERAPY: THE GERMAN NONINTERVENTIONAL ARATA STUDY

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Background: Depression is a common comorbidity in patients with RA and influences perception of disease activity and quality of life. We have previously reported that mean depression scores improved during TCZ therapy in conjunction with reductions in disease activity.¹

Objectives: To evaluate individual changes in depressive symptoms over 52 weeks in RA patients initiating treatment with TCZ.

Methods: We analyzed data from a large German multicenter observational study of patients with active RA who initiated TCZ therapy during routine clinical care (ML29087 ARATA study; NCT02251860). The Beck Depression Inventory-II (BDI-II), a self-report questionnaire for depression screening that has been validated in RA, was used to assess symptoms of depression. Patients were classified by baseline BDI-II scores into depression categories of no (BDI-II <14), mild (BDI-II 14-19), moderate (BDI-II 20-28), and severe depression (BDI-II ≥29).² Individual changes in BDI-II scores between baseline and week 52 were assessed. Erythrocyte sedimentation rate was used as the acute phase reactant in Disease Activity Score-28 joints (DAS28) assessments.

Results: Of 1155 patients enrolled from 108 clinical centers in Germany between May 2014 and July 2018, 474 completed the BDI-II at baseline (BDI-II cohort); baseline characteristics were similar to those of patients who did not complete the BDI-II. Approximately half of patients in the BDI-II cohort had BDI-II scores indicating no depression (248; 52.3%); the remaining patients had mild (87; 18.4%), moderate (84; 17.7%), or severe (55; 11.6%) depression. The mean (SD) baseline characteristics of the BDI-II cohort were 55.5 (12.5) yrs of age, 75.7% female, 10.6 (9.2) yrs RA duration, 4.9 (1.2) DAS28, and 24.3 (10.2) Clinical Disease Activity Index (CDAI). Baseline DAS28 and CDAI scores were similar among different depression subgroups, but patients with severe depression were more likely to be female (87.3% vs 70.6% for no depression) and had higher levels of anxiety, suicidal ideation, fatigue, pain, and sleep disturbance than patients with no or milder depression.

A total of 229 of the 474 patients (48.3%) in the BDI-II cohort completed the BDI-II at both baseline and week 52. At 52 weeks, the depression category of approximately half of patients with depressive symptoms at baseline changed to a lower level or no depression (Figure 1). Moderate to large improvements in BDI-II from baseline (>10 points) were reported by 33.3% to 38.5% of patients with baseline depressive symptoms (Figure 2).

Conclusion: At 52 weeks after initiating TCZ, the depressive disease burden was reduced. Future analyses with a representative patient cohort will be aimed at exploring whether improvements in depression occur independent of reductions in disease activity.

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Figure 1. Flow analysis of change in depression category for RA patients with completed BDI-II questionnaires at baseline and week 52 (n=229)

Figure 2. Improvement or deterioration of BDI-II scores over 52 weeks by BDI-II subgroup at baseline

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FRI0055

PREVALENCE OF CLINICALLY LATENT TUBERCULOSIS IN RHEUMATOID ARTHRITIS – A RETROSPECTIVE CLINICOPATHOLOGIC STUDY OF 161 AUTOPSY PATIENTS

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Background: The risk of tuberculosis (TB) is higher in rheumatoid arthritis (RA) than in the general population.

Objectives: The aim of this study was to determine the prevalence and histological characteristics of post-primary inactive or active TB in RA, to appraise the involvement of different organs, and to statistically assess the relationship between inactive and active TB in RA.

Methods: At the National Institute of Rheumatology 9475 patients died between 1969 and 1992; among them 161 with RA and all of them were autopsied.

RA was confirmed clinically according to the criteria of the ARA.

TB was detected at autopsy and specified histologically, retrospectively reviewing all available clinical and pathological reports.

Demographics of different patient cohorts were compared with the Student t-test. The relationship between inactive TB and active TB with miliary dissemination was analyzed with χ^2 -test.

Results: Post-primary TB was associated with RA in 21 (13.04%) of 161 patients. Post-primary TB was localized to the lung. Twelve (57.14%) of 21 TB were histologically only fibrous, pigmented (antracotic) tuberculous scars (fTB), and 9 (42.86%) of 21 revealed a fibrocaseous tubercle (fcTB). One of 12 fTB and 5 of 9

ftTB were associated with disseminated (miliary) tuberculosis (**mTB**) in 6 (3.7% of 161; 28.57% of 21) **RA** patients with **ftTB** or **ftTB**. Demographics, onset and duration of disease of 161 **RA** patients with **TB**, **ftTB**, **ftTB**, or **mTB** are summarized in Table.

Sex	Number of autopsies	Mean age in years at death $\pm$ SD	Range of age (in years)	Mean age at onset of disease $\pm$ SD	Disease duration (in years) $\pm$ SD
RA patients (total)	161	65.32 $\pm$ 12.95	16–88	50.83 $\pm$ 16.96	14.43 $\pm$ 10.51
without TB	140 of 161	64.77 $\pm$ 13.28	16–88	50.22 $\pm$ 16.99	14.36 $\pm$ 10.13
with TB	21 of 161	69.00 $\pm$ 9.70	50–84	54.19 $\pm$ 16.39	14.81 $\pm$ 12.41
with fibrous TB	12 of 21	70.92 $\pm$ 8.48	59–84	52.33 $\pm$ 16.01	18.58 $\pm$ 12.76
with fibrocasseous TB	9 of 21	66.44 $\pm$ 10.59	50–80	56.67 $\pm$ 16.55	9.78 $\pm$ 9.91
with miliary TB	6 of 21	68.33 $\pm$ 11.09	50–82	58.67 $\pm$ 8.24	9.67 $\pm$ 4.85

The mean age of **RA** patients was higher with **TB**, **ftTB**, **ftTB** or **mTB** in comparison to total population or to the patients without **TB**, but the difference was only significant between patient cohorts with **ftTB** and **RA** patients without **TB** (70.92 years versus 64.77, $p < 0.043$).

There was a definitely shorter duration of **RA** in patients with **ftTB** or **mTB** compared to the total population.

Proliferative or exudative epithelioid granulomatous **mTB** involved different organs, such as lung in 5, liver in 3, spleen in 2, lymph nodes in 2, adrenal gland in 1, synovial membrane in 1, vertebrae in 1 and pituitary gland in 1 of 6 **RA** patients with active **mTB**.

There was a significant correlation between: **TB** and **mTB** ($c=1$, $\chi^2=33.96$, $p<0.00000001$), **TB** and **ftTB** ($c=1$, $\chi^2=78.36$, $p<0.00000001$), **TB** and **ftTB** ($c=1$, $\chi^2=55.69$, $p<0.00000001$), or **ftTB** and **mTB** ($c=0.99$, $\chi^2=56.89$, $p<0.000001$). The link between **ftTB** and **mTB** was not significant ($c=0.45$, $\chi^2=0.007$, $p<0.9333$ – NS).

Conclusion: **TB**, **ftTB**, **ftTB**, or **mTB** complicated **RA** in both sexes, and at any time in the course of the disease.

The mean age at death was higher in all forms of **TB**. Significant difference was only in mean age of **ftTB** compared to the patients' cohort without **TB**. Fibrocasseous tubercle or miliary dissemination of tuberculosis reduced definitely the survival time (and disease duration) of aged **RA** patients.

Post-primary **TB** especially **ftTB** (mostly in the lungs) represents a high risk of miliary dissemination in **RA**. In our autopsy material **mTB** was the consequence of endogenous exacerbation of **TB** (and was not due to an exogenous reinfection), based on the high values of Youle's association coefficients between **TB** or **ftTB** and **mTB**.

The **mTB** may be considered as a terminal phenomenon, because of the limited numbers of granulomas involving only a few organs. The exudative character – beside proliferative epithelioid granulomas – must be regarded as histological evidence of impaired immune reactivity, an unfavorable prognostic sign in elderly patients, forecasting the possible fatal outcome of **RA** associated **TB**.

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FRI0056 LUNG COMPROMISE SCREENING IN PATIENTS WITH EARLY RA. A MULTICENTRIC CROSS SECTIONAL STUDY

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Background: Rheumatoid arthritis (RA) affects 0.4-1.3% of general population (1). It can affect lungs in different ways, with interstitial lung disease (ILD) as the most severe. Clinically evident ILD has been reported in 10-42% of patients, with a great impact in prognosis (2).

Objectives: To identify the prevalence of lung involvement in early rheumatoid arthritis patients (ERA) without previous known lung disease and describe the association between high resolution computed tomography (HRCT), lung functional tests (LFT) and clinical findings.

Methods: Cross sectional multicentric study. We included ERA patients (1 year or less since diagnosis) consecutively. Patients with previous RA related lung disease or biologic/targeted synthetic Dmard treatment were excluded. HRCT,

immunological tests (rheumatoid factor, anti-CCP, ANA), LFT and clinical evaluation were performed.

Results: We included 74 patients, 63 (85.1%) woman, mean (SD) of 47 (17.7) years. Thirty-seven patients (50%) were current or former smokers. Abnormal findings in HRCT were found in 62 patients (88.6%): ILD in 6 (8.6%), airway involvement in 40 (70%) and emphysema in 7 (10%). Ten patients (13.5%) had abnormal auscultation (2 sibilances, 2 roncus, and 6 crackles). Six patients (8.1%) had digital clubbing. Regarding immunological tests, 54/61 (88.5%) patients were positive for Anti CCP, and 53/61 (86.9%) were positive for RF. We compared features of patients with findings related to RA in HRCT (interstitial and/or airway) with those without them. We found no differences in the mean (SD) of DAS-28 [4.74 (1.38) vs 4.32 (1.39); $p=0.27$]. The prevalence of anti-CCP was not higher in patients with abnormal HRCT [38/44 (86.3%) vs 16/17 (94.1%); $p=0.39$]. Patients with abnormal HRCT were older [median (IQR) 50.5 years (44.5-59.5) vs 43 years (32-51); $p=0.008$] and showed higher VSG values [mean (SD) 39.09 (24.03) vs 27.38 (17.6); $p=0.043$]. Abnormal physical examination or dyspnea (class 2 mMRC or higher) was significantly associated with HRCT abnormalities [26 (50%) vs 3 (13.6%); $p=0.003$] and the presence of ILD on HRCT was significantly associated with crackles on the auscultation [4/68 (6.25%) vs 2/6 (33.33%); $p=0.023$].

Conclusion: This study shows a high prevalence of lung involvement in ERA patients of less 1 year from diagnosis. Also, we showed a significant association between HRCT and physical examination findings. This data highlights the importance of the clinical examination in Rheumatoid Arthritis patients. More studies with bigger samples and longitudinal follow up are needed to confirm and complete our results.

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FRI0057

A MODEL FOR QUANTIFYING THE EFFECT OF INFLAMMATION ON CARDIOVASCULAR DISEASE RISK PREDICTION IN RA PATIENTS

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Background: Patients with rheumatoid arthritis (RA) are at increased risk for cardiovascular disease (CVD)[1]. Quantifying the effect of inflammation on CVD risk is important because rheumatologists can reduce inflammation with effective RA medications. A new score has been developed for predicting the risk for a CVD event (MI, stroke or CV death) in RA patients. It combines serological measures of inflammation (the multi-biomarker disease activity [MBDA] score, a measure of RA disease activity; and three individual biomarkers [TNF-RI, MMP-3 and leptin]), with age and four conventional CVD risk factors (smoking, hypertension, diabetes and history of a high- risk CVD condition)[2]. To gain insight into the potential effect that treating inflammation may have on the CVD risk score, it would be useful to know how the score is affected by the level of inflammation.

Objectives: Explore the quantitative contribution of inflammation to CVD risk score in individual RA patients.

Methods: To quantify the effect of inflammation on the CVD risk score across a range of MBDA scores, a commercial dataset of 177,486 RA patients with ≥ 2 MBDA tests between October 2010 and June 2019 was split 2:1 into training and validation datasets. Curves showing variation in the CVD risk score across the spectrum of all possible MBDA scores (1-100) were generated for canonical patient types differing in the number of conventional risk factors (0 to 4) and age (45, 55, 65, 75, 85 years). To generate these curves, the contributions of TNF-RI, MMP-3 and leptin to the CVD risk score were treated in aggregate (denoted the molecular score) and estimated using a linear regression model of the difference in molecular scores vs. the difference in MBDA scores. This model for the molecular score was fit in the training dataset, then in the full dataset, with dataset (training or validation) and the interaction between dataset and change in MBDA score included as additional predictor variables. The method was considered validated if the F-test for the interaction variable was not significant at the 0.05 level.

Results: The model for estimating the molecular score from the MBDA scores was validated and shown to fit the data well (Figure 1). The estimated molecular