Interstitial lung disease in RMDs

OP0306 IMPACT OF INFLAMMATION ON INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS - AN ANALYSIS OF THE GERMAN BIOLOGICS REGISTER RABBIT

R. Ramien1,2, T. Rud1, M. Schneider3, S. Balzer6, A. Krause9, M. Schaefer1, Y. Meissner1, A. Strangfeld1.1 German Rheumatism Research Centre Berlin, Epidemiology and Health Services Research, Berlin, Germany; 2Charlottenburg, Department of Internal Medicine II, Berlin, Germany; 3Heinrich-Heine-Universität Düsseldorf, Rheumatology, Düsseldorf, Germany; 4Praxis Balzer, Rheumatologie, Bautzen, Germany; 5Immunkrankenhaus Abteilung für Innere Medizin/Schwerpunkt Rheumatologie, Rheumatologie, Berlin, Germany

Background: Ten percent of patients with prevalent rheumatoid arthritis (RA) develop an interstitial lung disease (ILD), which is associated with higher mortality (1). A previous study identified high/moderate disease activity, but not CRP, as a risk factor for RA-ILD (2).

Objectives: To analyse whether systemic inflammation (CRP and ESR) and/or disease activity measured with a composite score (DAS28-ESR) are associated with the occurrence of ILD in patients with RA.

Methods: Data from RA patients observed in the biologics register RABBIT until 10/2020 were included. Patients with incident ILD were selected as cases and matched 1:5 to controls using a modified risk-set sampling (controls had no ILD during the entire observation time). Matching criteria were age, sex, RA duration, date of enrolment and observation time. Odds ratios (OR) and 95% confidence intervals (CI) were computed by conditional logistic regression and adjusted for factors identified by a directed acyclic graph (DAG), namely smoking, rheumatoid factor (RF), chronic obstructive pulmonary disease, number of biologics until index date of ILD-diagnosis in cases, date after the respective observation time in controls) and mean glucocorticoid dosage (12 months prior index date). For the regression, CRP and ESR were log-transformed due to their skewed distribution, and missing values were addressed by multiple imputations (n=10).

Results: Out of 19,148 RA patients enrolled since 2001, 1,133 patients with incident ILD were identified. Half of the ILDs were diagnosed by computed tomography (n=67), 8% by x-ray (n=10) and in 42% the method was unknown (n=56). At baseline, cases and controls had a mean age of 61 years, 68% were female, and mean RA disease duration was 9 years. Differences were observed in smoking status (59% ever smokers in cases vs. 48% in controls), RF positivity (84% vs. 72%) and the sum of comorbidities (means 3.1 vs. 2.3). During the 12 months prior to the index date, mean values of CRP and especially of ESR were significantly higher in cases compared to controls. This difference was not observed for DAS28 (Figure 1, upper figures). Furthermore, more cases than controls were in a high inflammatory status, but not in at least moderate disease activity (Figure 1, lower figures). The adjusted regression analyses confirmed these results: CRP and ESR were significantly associated with incident ILD both at the time of diagnosis and in the 12 previous months, and results were even more pronounced with elevated CRP and ESR, which was not the case for DAS28 (Table 1).

Conclusion: In contrast to other data, our analyses found that markers of systemic inflammation, but not the DAS28 composite score, are associated with the occurrence of incident ILD in patients with RA and can be predictors for the development of RA-ILD. Therefore, in a treat-to-target approach, rheumatologists should pay particular attention to controlling systemic inflammation.

REFERENCES:
1. PMID: 20851924
2. PMID: 30951251

Acknowledgements: RABBIT is supported by a joint, unconditional grant from AbbVie, Amgen, BMS, Fresenius-Kabi, Galapagos, Hexal, Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis, Viatris and UCB.

Disclosure of Interests: Ronja Ramien: None declared, Tatjana Rudi: None declared, Matthias Schneider Speakers bureau: Astra-Zeneca; Biogen; BMS; Celgene; Chugai; GSK; Janssen-Cilag; Lilly; Pfizer; UCB. Paid instructor for: Lilly, Consultant of: Abbvie; Astra-Zeneca; Boehinger-Ingelheim; GSK; Lilly; Novartis; Pfizer; Protagen; Roche; Sanofi-Aventis; UCB, Grant/research support from: Abbvie; Astra-Zeneca; GSK; UCB, Sabine Balzer: None declared, Andreas Krause Speakers bureau: AbbVie, BMS, Boehinger Ingelheim, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Consultant of: AbbVie, BMS, Boehinger Ingelheim, Galapagos, Janssen, Lilly, MSD, Mylan, Novartis, Pfizer, Roche, Grant/research support from: AbbVie, UCB, Martin Schaefer: None declared, Yvette Meissner Speakers bureau: Pfizer, Anja Strangfeld Speakers bureau: AbbVie, Amgen, BMS, Celltrion, Janssen, Lilly, Pfizer, Roche, Sanofi, UCB.

DOI: 10.1136/rmdopen-2017-000619

Figure 1. Upper Figures. Unimputed and untransformed CRP, ESR and DAS28 12 months prior to the index date as means with 95% CI, computed by mixed models with matching strata as random effects. The left y-axis refers to CRP and ESR, the right to DAS28. Lower Figures. Percentages of patients with CRP≥5, ESR>21 and DAS28>3.2 12 months prior to the index date.

Table 1. Results of the conditional logistic regression for the risk of ILD.

<table>
<thead>
<tr>
<th>At index date</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log CRP</td>
<td>1.55 (1.25 – 1.92)</td>
<td>1.55 (1.24 – 1.94)</td>
</tr>
<tr>
<td>Log ESR</td>
<td>2.43 (1.55 – 3.81)</td>
<td>2.41 (1.49 – 3.88)</td>
</tr>
<tr>
<td>ESR&gt;21 vs. ESR≤21</td>
<td>1.56 (1.22 – 2.00)</td>
<td>1.56 (1.21 – 2.01)</td>
</tr>
<tr>
<td>DAS28</td>
<td>1.17 (1.01 – 1.35)</td>
<td>1.16 (0.99 – 1.35)</td>
</tr>
<tr>
<td>DAS28&gt;3.2 vs. DAS28≤3.2</td>
<td>1.31 (0.86 – 1.99)</td>
<td>1.32 (0.85 – 2.06)</td>
</tr>
</tbody>
</table>

Within 12 months prior to index date

| Log CRP      | 1.14 (1.14 – 1.75) | 1.38 (1.09 – 1.74)   |
| Log ESR      | 1.65 (1.26 – 2.16) | 1.60 (1.21 – 2.12)   |
| ESR>21 vs. ESR≤21 | 2.60 (1.54 – 4.41) | 2.60 (1.54 – 4.41)   |
| DAS28       | 1.16 (0.99 – 1.36) | 1.13 (0.95 – 1.34)   |
| DAS28>3.2 vs. DAS28≤3.2 | 1.37 (0.82 – 2.30) | 1.37 (0.79 – 2.35)   |

PULMONARY FIBROSIS IN EARLY RHEUMATOID ARTHRITIS IN RELATION TO GENETIC LOCI AND INDIVIDUAL ACA SPECIFICITIES

M. Brink1, L. Ljung2, M. Hansson1, J. Rönnefelt3, R. Holmdahl4, K. Skriver1, G. Serré5, L. Klareskog6, S. Fantappié Dahlqvist7.1 Umeå University, Public Health and Clinical Medicine, Rheumatology, Umeå, Sweden; 2Karolinska Institute, Medical Immunology, Inflammation Research, Department of Medical Biochemistry and Biophysics, Stockholm, Sweden; 3Charité, Universitätsmedizin, Berlin, Germany; 4Université de Toulouse, Institut Toulousain des Maladies Infectieuses et Inflammatoires, UMR 1291 Inserm, Toulouse, France

Background: Pulmonary manifestations in rheumatoid arthritis (RA) are common comorbidities but the underlying mechanisms are largely unknown. We found in a previous study 3 SNPs associated with pulmonary fibrosis (PF); rs3570950 (MUC5B), rs111521887 (TOLLIP), and rs2609255 (FAM13A) besides age, rheumatoid factor positivity and methotrexate treatment.

Objectives: To evaluate for the added value of a multiplex of anti-citrullinated peptide antibodies (ACPA) for the development of pulmonary fibrosis (PF) in an inception cohort of RA patients.

Methods: A total of 1184 patients with early RA were consecutively included and followed prospectively from the date of diagnosis (index date) until death or until 31 December 2016. The diagnosis of PF was based on high resolution tomography. The presence of 21 ACPA fine specificities were analysed in plasma sampled at index date, using a custom-made microarray chip (Thermo Fisher Scientific, Upsona, Sweden). Data on both ACPA and genetic data was available for 841 RA patients, of whom 50 developed PF. Associations were analysed using logistic regression analysis and presented as the odds ratio (OR) with the 95% confidence interval (CI). Models were adjusted for sex, age, DAS28 and presence of RF at RA diagnosis, smoking ever, and HLA-SE and in a second step for the three SNPs (.rs3570950, rs111521887 and rs2609255), respectively.
Results: In unadjusted analyses eight ACPA reactivities were found associated with PF development (p<0.05-0.001). The number of ACPA reactivities was related to PF development, both in crude and adjusted models (p<0.05 for both). In models concomitantly adjusted for the three SNPs (rs35705950, rs111521887 and rs2609255) respectively, in addition to mentioned adjustments the number of ACPA reactivities (p<0.05 for all three models), VimE60-75 (p<0.05, in all three models), Fjbi62–78 (72) (p<0.001-p<0.05) and F4-CIT-R (p<0.01-p<0.05) were all found significantly associated to PF development irrespective of the SNPs.

Conclusion: The development of PF in an inception cohort of RA patients was associated both with risk genes and, independently of the risk genes, the presence of certain ACPA, and the number of ACPA reactivities.

REFERENCES:

Acknowledgements: I have no acknowledgements to declare. The staff and patients at the departments of rheumatology in northern Sweden.

Disclosure of Interests: None declared

OP0308-HPR

MORE THAN HALF OF RA PATIENTS WITH A LIFETIME HISTORY OF MOOD DISORDERS WERE ANXIOUS AND DEPRESSED DURING THE COVID-19 PANDEMIC: RESULTS FROM THE CANADIAN EARLY COHORT (CATCH) STUDY

S. J. Bartlett1, O. Schier2, M. F. Valois3, G. Boire2, G. Hazlewood, C. Thorne5, D. Tin2, C. Hitchon6, J. Pope7, E. Keystone9, L. Bassette5, V. Bykerk5 on behalf of the CATCH investigators. 1McGill University & McGill University Health Centre, Medicine, Montreal, Canada; 2McGill University, Medicine, Montreal, Canada; 3University of Sherbrooke, Rheumatology, Sherbrooke, Canada; 4University of Calgary, Rheumatology, Calgary, Canada; 5Care, Rheumatology, Newmarket, Canada; 6University of Manitoba, Rheumatology, Winnipeg, Canada; 7Western University, Rheumatology, London, Canada; 8RheumKey, Rheumatology, Toronto, Canada; 9Laval University, Rheumatology, Quebec City, Canada; 10Hospital for Special Surgery, Rheumatology, New York, United States of America

Background: A growing number of studies indicate the considerable mental health impacts of the prolonged COVID-19 pandemic in the general population as chronic stress is a risk factor for the development of depression and anxiety. Mood disorders are more prevalent in RA and a history of anxiety or depressive disorders increases the risk of recurrence in the future.

Objectives: To compare trends in prevalence of anxiety and depressive symptoms, prior to and during the COVID-19 pandemic in RA patients with and without a lifetime history of mood disorders.

Methods: Data were from RA patients diagnosed and treated for RA in rheumatology clinics across Canada enrolled in the Canadian Early Arthritis Cohort (CATCH) Study. We estimated monthly trends in prevalence of clinically significant levels of anxiety and depression (PROMIS Depression and Anxiety 4a score 55+) from all visits between Mar 2019 and Jan 2022 and compared monthly trends in anxiety and depression in the year prior to (Mar 2019-Feb 2020) and during the pandemic (Mar 2020 to Jan 2021) stratified by lifetime history of mood disorders.

Results: 4,148 visits were completed from Mar 2019 to Jan 2022 in 1,644 RA patients with a mean (SD) age of 60 (14) and disease duration of 6 (4) years. 73% were women, 84% white, 60% had completed some post-secondary education, and 77% were in CDAI REM/LDA at the visit closest to the start of pandemic. 253 (15%) reported a lifetime history of depression and 217 (13%) a lifetime history of anxiety; 8% reported prior treatment for either.

Patients with a history of mood disorders had higher levels of depression and anxiety prior-to and during the pandemic compared with patients without a history of mood disorders (Table 1). Proportions were highest during COVID waves in all and were substantially higher and more variable in people with a previous history of mood disorders as compared to those without a history (Figure 1). While depressive symptoms peaked early in the pandemic, anxiety increased with each wave, peaking in Wave 3 (May-Jun 2021).

Table 1. Prevalence of depression and anxiety symptoms prior to and during the COVID-19 pandemic in RA patients with and without a history of mood disorders.

<table>
<thead>
<tr>
<th>Period</th>
<th>Prevalence (monthly range)</th>
<th>Depression</th>
<th>Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No history</td>
<td>Prior History</td>
</tr>
<tr>
<td>N observations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prepandemic (3/19 - 2/20)</td>
<td>35/27</td>
<td>62/1</td>
<td>36/10</td>
</tr>
<tr>
<td>Pandemic (3/20 - 1/22)</td>
<td>22/22</td>
<td>53/3</td>
<td>26/9</td>
</tr>
</tbody>
</table>

During the first 22 months of the COVID-19 pandemic, the proportion of patients with depression and anxiety increased in all groups. More than half of those with a history of emotional distress had clinically significant levels of depression and anxiety; proportions were highest during COVID waves in all and were substantially higher in people with previous history as compared to those without a history (see Figure 1). Whereas depressive symptoms peaked early in the pandemic, anxiety increased with each wave, peaking in Wave 3 (May-Jun 2021).

Conclusion: Symptoms of anxiety and depression were common in Canadian adults with RA prior to and after the onset of the COVID-19 pandemic. Whereas others have found that high levels of depression and anxiety occurred early in the pandemic but declined fairly rapidly in the general population, emotional distress was not attenuated over time in this large cohort of RA patients. Individuals reporting lifetime history of mood disorders were more than twice as likely to report anxiety and depression, with depression peaking early in the pandemic and anxiety growing with each successive wave in the first year. The results demonstrate the importance of applying a lifetime perspective as previous episodes of anxiety and depression may be an important marker of increased vulnerability and recurrence in RA patients, particularly during the pandemic.

REFERENCES:

Acknowledgements: CATCH is supported through unrestricted research grants from: Amgen and Pfizer Canada since 2007; Abbvie Corporation since 2011; Medexus since 2013; Sandoz Canada since 2019; Fresenius Kabi Canada since 2021 and; Organon Canada since 2021. Previous funding from Janssen Canada (2011-16); UCB Canada and Bristol-Myers Squibb Canada (2011-18); Hoffman La Roche Limited (2011-21); Sanofi Genzyme (2016-17); Eli Lilly Canada (2016-20); Merck Canada (2017-21) and; Gilead Sciences Canada (2020-21).

Disclosure of Interests: None declared

OP0309

WES ANALYSIS OF RARE FAMILIES POINTS TO A PATHOGENIC ROLE FOR THE CGAS/STING-TYPE I IFN AXIS IN SSC

P. Maus1, V. Smith2, T. Du Four2, M. Vazhnyue1, B. Lauwers4, N. Limaye3, 1De Duve Institute, ULouvain, Genetics of Autoimmune Diseases & Cancer (GEDI), Brussels, Belgium; 2Ghent University Hospital, Department of...