RA: Clinical aspects and comorbidities - II

OP0271  INCREASED RISK OF DEMENTIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONALWIDE POPULATION-BASED COHORT STUDY

Y. Eun1, K. D. Han1, S. Y. Kang1, S. Lee2, H. S. Cha3, E. M. Koh3, J. Lee3, H. Kim1,2, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Department of Internal Medicine, Seoul, Korea, Republic of South Korea; 2Soongsil University, Department of Statistics and Actuarial Science, Seoul, Korea, Republic of South Korea; 3Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medicine, Seoul, Korea, Republic of South Korea; 4Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medical Humanities, Seoul, Korea, Republic of South Korea

Background: There have been conflicting results of previous studies on the association between rheumatoid arthritis (RA) and the risk of dementia.

Objectives: In this study, we aimed to investigate the association between RA and dementia in a large nationwide population-based cohort.

Methods: Among patients diagnosed with RA between 2010 and 2017, patients who had undergone a national health examination within two years prior to RA diagnosis were included in the study (n = 138,592). Control group included age- and sex-matched non-RA controls who received a health check-up at the same time as RA patients (n = 692,960). The primary outcome of the study was incident dementia, which was defined by an ICD-10 code and the use of dementia medications. Kaplan-Meier curves and Cox proportional hazards regression analysis were used for the analysis.

Results: Mean follow-up duration of the study was 4.7 ± 2.2 years. RA patients had a 1.2 times higher risk of dementia than controls (adjusted hazard ratio [aHR] 1.19, 95% CI 1.16–1.23). In patients with RA, the aHR for Alzheimer’s disease (AD) was 1.21 (95% CI 1.17–1.25) and the aHR for vascular dementia (VD) was 1.10 (95% CI 1.09–1.12). In a stratified analysis according to age, gender, lifestyle factors and comorbidities, the association between RA and dementia was consistently found.

Conclusion: In a large nationwide population-based cohort, RA was associated with an increased risk of incident dementia. Appropriate evaluation of dementia is required when cognitive impairment occurs in RA patients. Further studies are warranted to identify mechanisms of increased risk of dementia in RA patients.

Disclosure of Interests: None declared.


OP0272  PREDNISONE USE AND THE INCIDENCE OF HYPERGLYCEMIA OR DIABETES IN PATIENTS WITH RHEUMATOID ARTHRITIS: A 10-YEAR SUB ANALYSIS OF THE BEST STUDY.

J. van der Pol1, S. A. Bergstra2, T. Huizinga3, C. Allaart1. 1Leiden University Medical Center, Rheumatology, Leiden, Netherlands

Background: Use of prednisone in rheumatoid arthritis has been questioned because it may trigger side effects such as hyperglycemia and diabetes.

Objectives: To assess whether in RA the use of prednisone is associated with the development of hyperglycemia and diabetes.

Methods: The BeST study is a multicenter, assessor-blinded randomized controlled 10-years follow-up trial in 508 non-diabetic early RA patients. Patients were randomised to 4 dynamic DMARD treatment strategy groups: 1) sequential monotherapy, 2) step-up combination therapy, 3) initial combination therapy including prednisone (60mg/day, tapered to 7.5mg/day in 7 weeks) and 4) initial combination therapy with infliximab. In groups 1, 2 and 4, prednisone had a maximum dose of 75mg/day by protocol. Treatment was steerred at disease activity score (DAS) ≤2.4. We performed a GEE over time to assess whether current prednisone use or cumulative prednisone dose were associated with hyperglycemia (glucose levels ≥7.8) and cox regression analyses to investigate the relationship between cumulative prednisone dose, previous prednisone use and diabetes (defined as either use of anti-diabetic medication or two instances of a glucose ≥11.1 in 3-months visits). All analyses were adjusted for potential confounders.

Results: In total, 33/508 patients (6.5%) developed diabetes during the trial; 12 of these (36%) had received prior treatment with prednisone (any dose). Median (IQR) duration of prednisone use in all 508 patients was 9 (15) months and cumulative doses ranged from 0 to 27942 mg. The mean cumulative dose ranged from 55.5 mg in group 1 to 6170.0 mg in group 3. Previous prednisone use or cumulative prednisone dose was associated with hyperglycemia or diabetes, with effect sizes ranging from a hazard ratio of 0.588 (95% CI 0.285; 1.21) for the association between any prednisone dose and diabetes to an odds ratio of 1.04 (95% CI 0.978; 1.13) for the association between cumulative prednisone dose and diabetes (Table 1). To identify potential causes for these results, we investigated the relationship between DAS and the same outcomes. We found a higher DAS was significantly associated with development of diabetes, but not with hyperglycemia.

Table 1. The relationship between prednisone dose, DAS and glucose levels, hyperglycemia and diabetes

<table>
<thead>
<tr>
<th>GEE</th>
<th>hyyperglycemia*</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any prednisone dose1</td>
<td>0.949</td>
<td>0.805; 1.29</td>
<td></td>
</tr>
<tr>
<td>Cumulative dose1</td>
<td>1.04**</td>
<td>0.978; 1.13</td>
<td></td>
</tr>
<tr>
<td>DAS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any prednisone dose2</td>
<td>0.959**</td>
<td>0.895; 1.02</td>
<td></td>
</tr>
<tr>
<td>Cumulative dose2</td>
<td>1.19, 95% CI 1.16–1.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cox Regression diabetes (any of the definitions)</td>
<td>HR</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>Any prednisone dose3</td>
<td>0.588</td>
<td>0.285; 1.21</td>
<td></td>
</tr>
<tr>
<td>Cumulative dose3</td>
<td>1.04**</td>
<td>0.978; 1.13</td>
<td></td>
</tr>
</tbody>
</table>

* = confidence interval. GEE: Generalized Estimated Equations, OR: odds ratio, HR: hazard ratio, DAS: disease activity* hyperglycemia: glucose level above 7.8 mmol/L; diabetes: random glucose level above 11.1 mmol/L at least two time points** *= odds ratio per 500mg cumulative prednisone increase: adjusted for DAS, age, diabetes and BMI; adjusted for cumulative prednisone dose, age, gender and BMI; adjusted for DAS, age and BMI

Conclusion: In early RA patients, cumulative dose nor any previous prednisone use was associated with the risk of hyperglycemia or diabetes. A higher DAS was significantly associated with increased risk of hyperglycemia and diabetes. Potential risks of prednisone may have been mitigated by suppression of DAS.

Disclosure of Interests: Joy van der Pol: None declared, Sytske Anne Bergstra Grant/research support from: Pfizer, Thomas Huizinga: None declared, Cornelia Allaart Grant/research support from: The BeSt study was supported by a government grant from the Dutch Insurance Companies, with additional funding from Schering-Plough B.V. and Janssen B.V.


OP0273  CHARACTERISTICS OF PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS IN FRANCE

S. Hecquet1,2, A. Combier2, A. Steelando2, M. Pons3, D. Wendling1, A. Moltò1,2, C. Miceli Richard3, Y. Allainore3, J. Avouac3, C. Hecquet1,2, A. Combier3, A. Steelandt3, M. Pons3, D. Wendling1, A. Moltò1,2, S. Hecquet1,2

Background: Recently, EULAR has proposed a definition of difficult-to-treat rheumatoid arthritis (D2TRA). However, descriptive data on D2TRA are scarce and only one Japanese publication details the D2TRA encountered in routine practice, no similar work has been done in Europe so far.

Objectives: To describe D2TRA patients encountered in France according to two definitions and evaluate their therapeutic responses to different targeted therapies.

Methods: We reviewed all patients with RA treated in day hospital at Cochin University Hospital between 2020 and 2021. We divided our population into two groups of patients, a D2TRA group and a non-D2TRA group. This division was made on the same population according to two different definitions of D2TRA, resulting in four patient groups. The first definition is the one proposed by EULAR (EULAR D2TRA) defining D2TRAs as RAs with failure of ≥2 bDMARDs (with different mechanisms of action) after failing csDMARD therapy. The second defined as D2TRA patients who have failed at least two targeted therapies, without pre-judging the mechanism of action (non-EULAR D2TRA). We analyzed clinical characteristics and evaluated their response to different targeted therapies. Disease activity was assessed using the DAS for 28 joints (DAS28) at the latest visit.

Results: In total, we included 320 patients, we identified 76 EULAR D2TRA patients (mean age 59 years, 87% female) with 244 of corresponding non-DTRA patients (mean age 60 years, 85% female) and 120 non-EULAR D2TRA patients (mean age 58.7 years, 87% female) with 200 of corresponding non-DTRA (mean age 61 years, 85% female). Compared to non-D2TRA patients, there were significantly more D2TRA patients from low socioeconomic backgrounds in both D2TRA groups. In the EULAR-D2TRA group, compared to the non-D2TRA, there were significantly more patients with diabetes (14% vs 6%, p=0.024). D2TRA patients in both groups had significantly more rheumatoid factor (RF), interstitial lung disease (ILD) and a higher DAS28 than non-D2TRA patients. No difference was noted regarding ACPA and erosions. We observed a lower proportion of remission in both D2TRA groups than in non-D2TRA group (21% in EULAR D2TRA vs 24% in non-D2TRA, p=0.034 and 23% in non-EULAR D2TRA vs 36% in non-D2TRA, p=0.024). There were significantly fewer patients on Methotrexate in the non-EULAR D2TRA group compared to the non-D2TRA group (53% vs 64%, p=0.046). In the non-EULAR D2TRA group, there were significantly more patients in remission on Rituximab than on TNF inhibitors (41% vs 5%, p=0.0032). We did not observe a significant difference in achieving remission in patients on JAK inhibitors or IL-6 inhibitors in the two groups of D2TRA.