The impact of disease activity and pain level in rheumatoid arthritis (RA) patients

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Background: Rheumatoid arthritis (RA) is a disabling and progressive chronic autoimmune disease with associated burden in terms of work disability.

Objectives: To investigate the impact that RA associated pain and disease activity have on the level of work impairment patients experience, using data from the Burden of Rheumatoid Arthritis across Europe: A Socioeconomic Survey (BRASS).

Methods: Data were extracted from BRASS, a societal perspective observational RA dataset across 10 European countries (EUS, Denmark, Sweden, Hungary, Poland and Romania). 476 RA specialist clinicians provided information on 4,079 adult patients; of these, 2,087 patients completed corresponding questionnaires. Analyses were conducted using data from the Work Productivity and Activity Impairment Questionnaire, which is a patient-reported measure of work impairment.

Results: Of the 464 included in the analysis, average age was 54.6(14.1) years; mean (standard deviation); average DAS28-CRP score was 3.1(1.2), and average disease duration was 7(10) years; median (interquartile range). Descriptive analysis indicated that with greater levels of pain and/or disease activity, patients suffered increased levels of both work and activity impairment. The average marginal effect of covariates was calculated from regression outputs. Both pain level and DAS28-CRP score independently had a statistically significant association with work impairment; a unit increase in DAS28 score meant an increase in work impairment of 4.7% (p=0.011), whereas existence of ‘mild’, ‘moderate’ or ‘severe pain’ versus ‘no pain’ increased impairment by 33.3%, 43.4% and 45.0% respectively (p<0.05), with confounders age, gender, BMI and either DAS28-CRP or pain level held constant.

Conclusions: Results from this large, multinational survey in Europe show that subjective domains of the disease, such as pain, could be as important as objective measures of RA activity in affecting a patient’s ability to work; analysis suggested both pain and severity independently have a significant impact on work and activity impairment due to RA.

Disclosure of Interest: None declared

we analyzed data from the study visit with higher disease activity from each patient, applying multivariate linear regression analysis, with PGA as dependent variable/gold-standard. Independent variables tested in the models included items from SLEDAI-2K and continuous variables for swollen joint count, proteinuria, platelet and white blood cells counts. Some features absent from SLEDAI, such as hemolytic anemia, gastrointestinal and cardiopulmonary involvement were added to the model. To assess correlation validity we performed a Spearman’s correlation between the SLE-DAS, PGA and SLEDAI-2K at last follow-up visit. We tested performance of SLEDAI-2K (change >4) and SLE-DAS to discriminate a clinically meaningful worsening and improvement in SLE disease activity (change in PGA ≥0.3) using Receiver Operating Characteristic (ROC) curve analysis. We determined the best cut-offs values of SLE-DAS to detect changes in PGA ≥0.3 and calculated the sensitivity, specificity, positive and negative predictive values (PPV, NPV). Statistical significance was set at 0.05.

Results: The final SLE-DAS model included 17 items. The SLE-DAS score at last follow-up visit presented high correlation with PGA (rho=0.975, p<0.0005) and SLEDAI-2K (rho=0.94, p<0.0005). For improvement in PGA ≥0.3, in ROC analysis a change in SLE-DAS presented a much higher performance [area under curve (AUC)=0.927 (95% CI=0.885–0.969, p<0.0005)] than SLEDAI-2K [AUC=0.787 (95% CI=0.718–0.857), p<0.0005] (figure 1). For worsening of PGA ≥0.3, change in SLE-DAS and SLEDAI-2K presented an AUC of 0.949 (95% CI=0.988–1.000, p<0.0005) and 0.914 (95% CI=0.870–0.959, p<0.0005), respectively (figure 1). The optimal discriminative cut-off for either a PGA increase or reduction was change in SLE-DAS ≥1.72 (table 1).

Table 1: Performance of SLE-DAS and SLEDAI-2K to detect change in SLE disease activity.

<table>
<thead>
<tr>
<th>PG ≥0.3</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement PGA ≥0.3</td>
<td>82.1</td>
<td>96.9</td>
<td>87.3</td>
<td>95.4</td>
<td>44.8</td>
<td>96.5</td>
<td>76.9</td>
<td>87.0</td>
</tr>
<tr>
<td>Worsening PGA ≥0.3</td>
<td>93.1</td>
<td>97.7</td>
<td>90.0</td>
<td>98.5</td>
<td>46.6</td>
<td>99.6</td>
<td>96.4</td>
<td>89.5</td>
</tr>
</tbody>
</table>

Sens: Sensitivity (%); Spec: Specificity (%); PPV: Positive predictive value (%); NPV: Non predictive value (%).

Conclusions: The SLE-DAS presents good construct validity and much higher discriminative power to detect changes in SLE disease activity as compared to SLEDAI-2K. External validation in another SLE cohort is underway.

Disclosure of Interest: None declared.

References:


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Conclusions: In conclusion, we found that autoantibody status was not associated with early remission in newly diagnosed RA-patients receiving methotrexate in real-world clinical practice. These results do not support the hypothesis that treatment should be tailored to “autoantibody status” when it comes to initiating methotrexate therapy as first-line anti-rheumatic treatment. Rather, our results indicate that that methotrexate is effective as primary anchor drug regardless of autoantibody status.

Disclosure of Interest: None declared


THE USE OF MRI-DETECTED SYNOVITIS TO DETERMINE THE NUMBER OF INVOLVED JOINTS FOR THE 2010 ACR/EULAR CLASSIFICATION CRITERIA FOR RHEUMATOID ARTHRITIS – IS IT OF ADDITIONAL BENEFIT?

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Background: The 2010 ACR/EULAR classification criteria have been developed, as early classification of Rheumatoid Arthritis (RA) is important. The 2010-criteria states that imaging can be used to determine the number of joints with synovitis. This seems reasonable as previous studies on Magnetic Resonance Imaging (MRI) in early arthritis patients have shown that synovitis is present in a substantial number of joints that were neither swollen nor tender at clinical examination. Although development of the 2010-criteria was primarily data-driven, the suggestion to also use advanced imaging modalities to detect synovitis was based on expert opinion. Scientific data supporting the use of MRI is lacking.

Objectives: To assess the value of MRI-detected synovitis to determine the number of involved joints on the performance of the 2010-ACR/EULAR classification criteria for RA.

Methods: 277 consecutive patients with a clinical diagnosis of RA or undifferentiated arthritis (UA) were studied. They underwent contrast enhanced 1.5T MRI of MCP-, wrist- and MTP-joints at baseline. Two outcomes were studied after 1 year follow-up: disease modifying anti-rheumatic drugs (DMARD)-initiation and fulfilling the 1987-criteria. Test characteristics were calculated when the number of involved joints was determined with and without MRI-detected synovitis.

Results: At baseline, 143 of 277 patients did not fulfil the 2010-criteria when the number of involved joints was determined by clinical evaluation of swelling and tenderness. When MRI-detected synovitis was also considered 69 patients had increased joint counts. Of these, 36 patients received more points for the item ‘number of involved joints’ and 14 reached ≥ 6 points and now fulfilled the 2010-criteria for RA. Thus, 10% of patients that were formally classified as UA were additionally classified as having RA.

Without considering MRI-detected synovitis, the sensitivity of the 2010-criteria was 62% and the specificity 90%, for DMARD initiation as outcome. With the addition of MRI-detected synovitis, the sensitivity increased to 67% and the specificity decreased to 84%. The AUC changed from 0.76 to 0.75. The net proportion of correctly reclassified patients was -2.4%. Of the additionally classified patients, 64% (9/14) were started on DMARDS and were considered true positives, whereas 36% (5/14) were not treated with DMARDS and developed alternative clinical diagnoses during the first year.

Results for the outcome 1987-criteria fulfilment after 1-year were similar. The sensitivity changed from 79% to 81% and the specificity from 78% to 71% the proportion or correctly reclassified patients was -5.1%.

Conclusions: To our knowledge, this study is the first providing evidence on the value of MRI-detected synovitis in addition to tender and swollen joints for the classification of RA. We did not find an increased accuracy of the 2010 criteria when incorporating MRI-detected synovitis. Further research on this subject in other longitudinal cohorts is needed, but at present there is no scientific proof that MRI-detected synovitis is of additional benefit for classifying RA.

Disclosure of Interest: None declared


SYNOVIAL TISSUE HISTOPATHOLOGY FINDINGS IN EARLY RA. IS IT USEFULL? ANALYSIS OF THE BELGIAN CAP46 COHORT.

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Background: The development of ultrasound-guided synovial biopsy will enable synovial tissue collection from small joints and will facilitate histopathological studies, thus improving the understanding of early rheumatoid arthritis (ERA). The CAP46 cohort is an original multicentre prospective observational study of early inflammatory joint diseases (IJD). The CAP46 cohort is an original multicentre prospective observational study of early inflammatory joint diseases (IJD).

Conclusions: Anti-drug antibodies (ADAb) to biological drugs predispose patients to low drug levels and lack of treatment response. For certolizumab pegol (CP) knowledge about the frequency and clinical relevance of ADAb is limited in patients with inflammatory joint diseases (UD).

Objectives: To assess the frequency and clinical relevance of early ADAb development in patients with inflammatory joint diseases treated with CP.

Methods: Patients from the NOR-DMARD study (n=310) with a clinical diagnosis of rheumatoid arthritis (RA, n=91), psoriatic arthritis (PsA, n=61), axial spondylarthritis (axSpA, n=116) and other UD (42) starting treatment with CP, who had available biobank sample at 3 months follow-up, were included. Serum samples are non-tough samples collected at 3 months. Drug concentrations were analysed using an in-house immunofluorometric assay automated on the AutoDELFA immunoassay platform. ADAb was detected by a primary assay measuring neutralising ADAb and two confirmational tests (antigen-bridging test and a 3-step immunofluorometric assay). Patients with RA, PsA and axSpA were included in response analyses. Treatment response was defined by EULAR good/moderate response in RA, DAS28 improvement ≥0.6 in PsA, and ASDAS clinically important improvement (CI) in axSpA.

Results: After 3 months of treatment, 19 of 310 (6.1%) patients were ADAb positive (5 RA, 4 PsA, 6 axSpA and 4 other UD). ADAb positive patients had significantly lower CP levels than ADAb negative patients, median 1.0 (IQR 0.2–6.8) vs 34.4 (IQR 21.2–44.7) mg/L (P<0.001). Response data were available for 245 patients. Of these, only 11/9 (12%) ADAb-positive patients was classified as a responder, while 10/11 (91%) were non-responders. Among ADAb-negative patients with response data, 129/234 (55%) were responders, while 105/234 (45%) were non-responders.

Conclusions: ADAb against CP were detected in 6.1% of patients after 3 months of treatment and were associated with low drug levels and reduced treatment response. These results suggest that drug levels and ADAb may be important for monitoring efficacy of treatment with TNF inhibitors, but the clinical significance needs to be examined in randomised clinical strategy trials.

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Anti-Drug Antibodies to Certolizumab Pegol Are Associated with Low Drug Levels and Reduced Clinical Response at 3 Months in Patients with Inflammatory Joint Diseases. Data from the NOR-DMARD Study.

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