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# Do Anti-Citrullinated Protein Antibodies and Anti-Sjögren's-Syndrome-Related Antigen A Double Positive Patients With Secondary Sjögren's Syndrome and RA Have Higher Joint Disease Activity?

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## Introduction

- Sjögren's syndrome associated with RA (sSS) is considered an extra-articular manifestation of RA and is an autoantibody-mediated condition similar to RA.
- Based on a 2006 study that used Larsen scores to quantify wrist damage, an association was seen between joint destruction in patients with RA and a dry mouth or a positive labial salivary gland biopsy (sSS patients).[1]
- Anti-citrullinated protein antibody (ACPA) positivity is associated with more severe joint damage. Patients with sSS could be ACPA and anti-Ro/Sjögren's syndrome–related antigen A (SSA) double positive.
- There are limited data on the impact of double positivity of ACPA and SSA on RA disease burden.
- Therefore, it is of interest to analyze patients with sSS with RA with higher levels of antibodies of ACPA and SSA.

### Objective

- To compare patients with RA with sSS with and without double positivity.

## Methods

- Data from adult patients with RA enrolled in a longitudinal RA registry were analyzed.
- Patients in the registry were evaluated annually by a rheumatologist for disease activity and treatment, and semi-annually on multiple clinical patient-reported outcomes (PROs) and resource utilization parameters.
- Patients with sSS were identified with a clinician's diagnosis or based on meeting the 2016 ACR/EULAR classification of primary Sjögren's syndrome.
- Patients with sSS were divided into two mutually exclusive groups: patients with and without double positivity (the latter including single positive or double negative patients).
- The two cohorts were compared using descriptive statistics to summarize baseline differences in demographics, disease activity measures, serostatus and treatments.
- A Kruskal–Wallis test for continuous variables and a chi-square test for categorical variables were performed with a significance level of 0.05.
- Disease activity in the follow-up was measured at the 12-month mark with a window of 6 months on either side. In case of multiple measurements in the window, an average of the measurements was taken as the follow-up disease activity score (Figure 1).
- Mean changes from baseline to 12 months in disease activity measures and PROs were assessed for patients with available data at baseline and follow-up.

**Figure 1. Study Design**

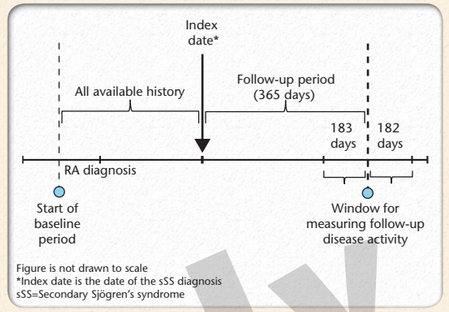


Figure is not drawn to scale
*Index date is the date of the sSS diagnosis
sSS=Secondary Sjögren's syndrome

## Results

- A total of 415 patients were identified as having sSS associated with RA, with 80 (19.3%) patients with double positivity and 86 (20.7%) patients without double positivity; 249 (60.0%) patients did not have information available for either ACPA or SSA tests.
- The patients with double positivity with sSS were diagnosed with RA at a younger age, had longer duration since onset of RA symptoms, and a higher number of swollen joints compared to patients with sSS without double positivity (Table 1).
- In addition, the mean changes in disease activity were lower in patients with versus without double positivity, though these were not statistically significant, potentially due to the limited sample size (Table 2).

**Table 1. Baseline Characteristics of Patients With sSS With and Without ACPA and SSA Positivity**

| | sSS patients with double positivity | | sSS patients without double positivity* | | p value |
|---|---|---|---|---|---|
| | N | Mean (SD) | N | Mean (SD) | |
| Age, years | 80 | 54.6 (13.9) | 86 | 55.1 (13.5) | 0.683 |
| Age at RA diagnosis, years | 80 | 41.3 (14.3) | 85 | 48.7 (13.5) | 0.001 |
| RA symptoms duration, years | 80 | 15.3 (12.8) | 85 | 10.0 (10.5) | 0.001 |
| Female, n (%) | 80 | 74 (92.5) | 86 | 79 (91.9) | 0.878 |
| BMI | 71 | 27.5 (7.6) | 69 | 27.6 (5.9) | 0.388 |
| RADAI | 72 | 4.0 (2.4) | 80 | 4.0 (2.1) | 0.896 |
| DAS28 (CRP) | 66 | 4.0 (1.8) | 69 | 3.5 (1.4) | 0.072 |
| CDAI | 64 | 25.1 (19.2) | 67 | 17.9 (13.6) | 0.065 |
| SJC | 74 | 7.4 (7.5) | 76 | 4.0 (5.3) | 0.002 |
| TJC | 74 | 9.3 (9.3) | 76 | 6.2 (6.5) | 0.105 |
| MDHAQ fatigue scale | 72 | 47.4 (30.4) | 80 | 53.5 (29.9) | 0.252 |
| Comorbidities, n (%) | | | | | |
| Vasculitis, cutaneous | 80 | 7 (8.8) | 86 | 0 (0.0) | 0.005 |
| Vasculitis, other | 80 | 2 (2.5) | 86 | 1 (1.2) | 0.609 |
| Lymphoma | 80 | 1 (1.3) | 86 | 0 (0.0) | 0.482 |
| Neuropathy | 80 | 2 (2.5) | 86 | 4 (4.7) | 0.683 |
| Lung cancer | 80 | 0 (0.0) | 86 | 1 (1.2) | 1.000 |
| Pulmonary fibrosis | 80 | 1 (1.3) | 86 | 0 (0.0) | 0.483 |
| Pulmonary nodules | 80 | 3 (3.8) | 86 | 1 (1.2) | 0.353 |

Values are mean (SD) unless otherwise stated
*Includes single positive and double negative patients
ACPA=anti-citrullinated protein antibodies; MDHAQ=Multidimensional Health Assessment Questionnaire; RADAI=Rheumatoid Arthritis Disease Activity Index; SSA=Sjögren's-syndrome-related antigen A; sSS=secondary Sjögren's Syndrome

**Table 2. Change in Disease Activity Measures and Fatigue at 12 Months**

| | 12 months | | Change from baseline | | |
|---|---|---|---|---|---|
| | sSS patients with double positivity | sSS patients without double positivity* | sSS patients with double positivity | sSS patients without double positivity* | p value |
| RADAI | 3.7 (2.3) n=64 | 3.6 (2.0) n=70 | –0.3 (2.0) n=64 | –0.2 (1.4) n=70 | 0.427 |
| DAS28 (CRP) | 3.9 (1.8) n=47 | 2.8 (1.2) n=50 | –0.1 (1.6) n=47 | –0.6 (1.3) n=50 | 0.149 |
| CDAI | 23.0 (20.6) n=47 | 12.5 (11.1) n=45 | –0.8 (19.8) n=47 | –4.2 (12.3) n=45 | 0.702 |
| SJC | 6.7 (8.2) n=60 | 1.9 (4.1) n=59 | –1.0 (7.6) n=60 | –1.7 (4.0) n=59 | 0.911 |
| TJC | 7.7 (8.4) n=60 | 3.6 (5.7) n=59 | –1.3 (8.7) n=60 | –2.1 (6.4) n=59 | 0.808 |
| Total joint count | 14.4 (16.5) n=60 | 5.6 (8.3) n=59 | –2.2 (15.2) n=60 | –3.7 (8.9) n=59 | 0.934 |
| Fatigue scale | 49.2 (27.4) n=64 | 46.9 (24.9) n=69 | 2.1 (24.5) n=64 | –5.6 (21.0) n=69 | 0.082 |

Value are mean (SD)
*Includes single positive and double negative patients
ACPA=anti-citrullinated protein antibodies; RADAI=Rheumatoid Arthritis Disease Activity Index; sSS=secondary Sjögren's Syndrome

## Conclusions

- Patients with sSS with double positivity versus without double positivity for ACPA and SSA had greater RA disease burden at baseline.
- Greater RA disease burden after 12-month follow-up was also observed for the sSS patients with double positivity compared to sSS patients without double positivity.
- Further analysis with a larger sample size is warranted.

## Reference

1. Marotte H, et al. *Ann Rheum Dis* 2006;**65**:905–9.

## Acknowledgments

This study was sponsored by Bristol-Myers Squibb. The authors thank Michelle Frits for support with the study. Editorial assistance was provided by Mary Casey and Michele Springer at Caudex and was funded by Bristol-Myers Squibb.

## Disclosures

EA and YB: shareholders and employees: Bristol-Myers Squibb.
YS and AR: consultancy fees: Mu Sigma. CKI: none declared.
MEW: grant/research support: Amgen, Bristol-Myers Squibb, Crescendo Bioscience and Sanofi/Regeneron; consultancy fees: AbbVie, Ablynx, Amgen, Bristol-Myers Squibb, Can-Fite, Corrona, Crescendo, GlaxoSmithKline, Gilead, Lilly, Lycera, Merck, Momenta, Novartis, Pfizer, Roche, Samsung, Set Point, UCB and Vertex.
NS: grant/research support: Amgen, Bristol-Myers Squibb, Mallinckrodt and Sanofi-Regeneron; consultancy fees: Bristol-Myers Squibb.