

RAPID3 correlates with ESSPRI and other patient-reported outcomes in patients with primary Sjögren's syndrome

Sirs,
Therapeutic strategies for primary Sjögren's syndrome (pSS) are currently mainly empirical. In recent years, biological therapies, in particular those targeting B-cells or co-stimulation, have been studied in pSS patients with some encouraging results (1). When using biological therapies, reliable measures of treatment response, such as the EULAR Sjögren's syndrome patient-reported index (ESSPRI) (2), and the EULAR Sjögren's syndrome disease activity index (ESSDAI) (3), are of crucial importance. There is a need to identify specific subsets of pSS patients that would benefit from targeted treatments. Joint symptoms are among the commonest extraglandular manifestations of pSS, the prevalence of arthralgias being 55%, and that of arthritis 35% in a large pSS patient cohort from Spain (4). Although representing just one area of the wide spectrum of extraglandular symptoms of pSS, the impact of joint symptoms in treatment decisions is no doubt significant.

The Routine Assessment of Patient Index Data 3 (RAPID3) and its electronic counterpart eRAPID3, simple measures to evaluate activity of joint symptoms in rheumatoid arthritis (RA) patients in daily clinical practice, were recently thoroughly reviewed by Pincus (5). RAPID3 includes three self-reported scores (physical function, pain and patient global estimate), each scored 0–10 (5). In addition to RA, RAPID3 has also been tested in other patient groups and it has been found applicable also in patients with ankylosing spondylitis, psoriatic arthritis and SLE (6). The feasibility of RAPID3 has, however, not been studied in patients with pSS.

We aimed here to study the correlations of RAPID3 with ESSPRI, the specific patient reported outcome for pSS, and with immunological parameters in patients with pSS. To this end, we used our recently reported data on one hundred consecutive outpatient visits of pSS patients (7–8), who had answered the ESSPRI questionnaire and fulfilled at least four of the revised American-European consensus group criteria (9). RAPID3 values were calculated from the MDHAQ (multi-dimensional health assessment questionnaire) of these subjects. Data on the RAPID3 (range 0–30), the ESSPRI (0–10 cm), patient's global health assessment (visual analogue scale, 0–10 cm) (PGH-VAS), pain-VAS (0–10 cm) and HAQ (range 0–3) were gathered from the patient charts. The pSS patients were further classified according to pre-specified RAPID3 severity levels (5).

Table I. Correlation (r) of RAPID3 with clinical and immunological findings during 69 pSS outpatient visits (Spearman correlation coefficient).

Variable	r for RAPID3	p-value
Age	0.135	0.269
Disease duration	0.287	0.021
BMI, n=67	0.004	0.977
ESSPRI	0.718	<0.0001
Pain-VAS	0.878	<0.0001
PGH-VAS	0.843	<0.0001
HAQ	0.604	<0.0001
ESR	0.214	0.077
Blood haemoglobin	-0.058	0.634
Blood leukocytes	0.190	0.118
Serum beta-2 microglobulin, n=62	0.019	0.882
Serum IgG, n=58	0.004	0.974
Serum IgA, n=56	0.211	0.118
Serum IgM, n=56	-0.055	0.685
Serum C3, n=55	0.166	0.226
Serum C4, n=55	-0.043	0.758

RAPID3: Routine Assessment of Patient Index Data 3; pSS: primary Sjögren's syndrome; BMI: body mass index; ESSPRI: EULAR Sjögren's syndrome patient-reported index; VAS: visual analogue scale; PGH: patient's global health assessment; HAQ: Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate.

RAPID3 data were available from 69 of the 100 outpatient visits (63 female, 6 male). The mean age of the 69 pSS patients was 53±13 years, and the mean duration of the disease was 9±9 years. The articular domain of the ESSDAI showed moderate activity in 4% and low activity in 22% of the outpatient visits. Hydroxychloroquine was in current use in 55%, glucocorticoids in 34% and methotrexate in 7% of the patients. The median RAPID3 level in this pSS patient cohort was 2.00 (interquartile range (IQR) 0.50–6.45), which is lower than previously reported in cohorts of other rheumatic diseases (6). Nine (13%) of the patients showed a high, 17 (25%) a moderate, 12 (17%) a low and 31 (45%) an inactive RAPID3 level.

RAPID3 correlated significantly with disease duration, ESSPRI, PGH-VAS, pain-VAS and HAQ in patients with pSS (Table I). pSS patients with high or moderate RAPID3 activity (≥6.1) had significantly higher ESSPRI levels than the others (5.9 cm (IQR 4.3–6.7) vs. 3.0 cm (IQR 1.7–4.0), $p<0.0001$, Mann Whitney U-test).

RAPID3 was demonstrated here to correlate well with the pSS-specific patient reported outcome measure, ESSPRI, but no correlations were observed between RAPID3 and immunological parameters. Similar to our results with RAPID3 and ESSPRI, a recent Dutch study discovered a significant correlation between the arthritis activity index DAS-28 with the articular domain of the ESSDAI in pSS patients (10).

To conclude, RAPID3 might be a useful tool in addition to ESSPRI in the evaluation of treatment effects on articular involvement

in pSS patients. However, to evaluate other systemic symptoms and immunological activity of pSS, determination of the ESSDAI is necessary.

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References

1. FERRO F, VAGELLI R, BRUNI C *et al.*: One year in review 2016: Sjögren's syndrome. *Clin Exp Rheumatol* 2016; 34: 161–71.
2. SEROR R, RAVAUD P, MARIETTE X *et al.*: EULAR Sjögren's syndrome patient reported index (ESSPRI): development of a consensus patient index for primary Sjögren's syndrome. *Ann Rheum Dis* 2011; 70: 968–72.
3. SEROR R, RAVAUD P, BOWMAN *et al.*: EULAR Sjögren's syndrome disease activity index: development of a consensus disease activity index for primary Sjögren's syndrome *Ann Rheum Dis* 2010; 69: 1103–9.
4. RAMOS-CASALS M, BRITO-ZERON P, SOLANS R *et al.*: Systemic involvement in primary Sjögren's syndrome evaluated by the EULAR-SS disease activity index: analysis of 921 Spanish patients (GEAS-registry) *Rheumatology* 2014; 53: 321–31.
5. PINCUS T: Electronic eRAPID3 (Routine Assessment of Patient Index Data): opportunities and complexities. *Clin Exp Rheumatol* 2016; 34 (Suppl. 101): S49–53.
6. CASTREJÓN I, NIKIPHOROU E, JAIN R, HUANG A, BLOCK JA, PINCUS T: Assessment of fatigue in routine care on a Multidimensional Health Assessment Questionnaire (MDHAQ): a cross-sectional study of associations with RAPID3 and other variables in different rheumatic diseases. *Clin Exp Rheumatol* 2016; 34: 901–9.
7. PERTOVAARA M, KORPELA M: ESSPRI and other patient-reported indices in patients with primary Sjögren's syndrome during one hundred consecutive outpatient visits at one rheumatological clinic. *Rheumatology* 2014; 53: 927–31.
8. PERTOVAARA M, KORPELA M: Regular physical activity is associated with lower levels of ESSPRI and other favorable patient-reported outcomes in patients with primary Sjögren's syndrome. *Clin Exp Rheumatol* 2016; 34: 560.
9. VITALI C, BOMBARDIERI S, JONSSON R *et al.*: Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis* 2002; 61: 554–8.
10. MOERMAN R, ARENDS S, MEINERS PM *et al.*: Detailed analysis of the articular domain in patients with primary Sjögren's syndrome. *J Rheumatol* 2017; 44: 292–6.