Correlation between ESSDAI and ClinESSDAI in a real-life cohort of patients with Sjögren's syndrome

Sirs,

Great efforts have been made to develop valid tools for the assessment of disease activity in Sjögren's syndrome (SS). An international project supported by EULAR developed consensus disease activity indexes: the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), and an index to assess systemic manifestations, *i.e.* the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). Both the EULAR indexes have been developed and validated in an international collaboration to be consensual. In addition, a third index, the ClinESSDAI, has been recently proposed for the assessment of the sole clinical activity in SS, and it resulted very close to the original ESSDAI (1, 2). The rationale for developing ClinESSDAI was to provide an accurate evaluation of disease activity independently of B-cell biomarkers (*i.e.* to detect clinical change independently from the biological effects of the drug) and also to allow clinical assessment when some laboratory features are not available, as may occur in clinical practice. Thus, ClinESSDAI did not include the biological domain of ESSDAI; it was elaborated by analysing 702 fictive vignettes derived from 96 real cases of primary SS already used for the ESSDAI development. Validation of the ClinESSDAI in a real-life cohort, different from that used for the ESSDAI development, is still lacking.

To this end, both the ESSDAI and ClinESSDAI scores were studied in a large multicentre cohort of 966 primary SS patients. All patients fulfilled the American-European Consensus Group Criteria for primary SS (3), and the ESSDAI and ClinESSDAI scores were calculated at SS diagnosis (4). The mean age of the patients was 52±14 years, and 95.4% were females. Anti-Ro/SSA and anti-La/SSB antibodies were positive in 684/966 (70.8%), and 353/966 (46.5%), respectively, while patients negative for both antibodies were 271 (28.1%). Rheumatoid factor, cryoglobulinaemia, low C3 or low C4 were detected in 490/953 (50.7%), 73/825 (7.6%), 193/961 (20%), and 115/961 (11.9%) patients, respectively. Details on data collection and laboratory methods were described elsewhere (5-7). The median ESSDAI and ClinESSDAI scores were the same in this series [5, (range 0–63), and 5 (range 0–60), respectively)]. Correlation between the ESSDAI and ClinESSDAI scores was evaluated by Spearman's test (Table I). Linear regression model was used in the multivariate analysis. The ClinESSDAI score significantly correlated with the ESSDAI score (p<0.0001, r=0.972) (Fig. 1). Both the ClinESDDAI and ESSDAI scores significantly correlated with all single domains of the ClinESSDAI and ESSDAI, respectively, showing very similar results, even if the level of correlation was moderate to low in all the domains for both tools (Table I).

Notably, ClinESSDAI significantly correlated even with the biological domain of the ESSDAI score (Table I). Correlations between the single clinical domains with ClinESSDAI remained significant also in the multivariate model (p<0.0001 for all clinical domains, except for "muscular" which showed p=0.001), while "biological" domain of the ESSDAI was not significant. Interestingly, focus score (median 2; range 0–12), which was available in 363/966 patients (37.6%), did not correlate with either the ClinESSDAI or the ESSDAI (p=0.63, and p=0.426, respectively), while a negative correlation was observed with age at diagnosis (p<0.0001, r=-0.151, for the ClinESSDAI; p<0.0001, r=-0.17, for the ESSDAI), *i.e.* younger patients showed a more active disease.

In conclusion, ClinESSDAI seems to be a valid tool to assess clinical disease activity in primary SS. Since ClinESSDAI correlated with the biological domain of ESSDAI, it suggests that clinical picture may mirror some biologic abnormalities in clinical practice. In addition, ClinESSDAI may be a useful secondary endpoint in clinical trials. In fact, when considering novel therapeutic interventions (8, 9) and the time to evaluate the response, discrepancies between clinical and biologic outcomes might occur in SS (2), as in lupus (10), with novel targeting drugs showing particular efficacy on biologic biomarkers of disease.

Table I. Single domain correlations with ESSDAI and ClinESSDAI.

	ESSDAI		ClinESSDAI	
Domain (rate)	p-value	Spearman's rho	p-value	Spearman's rho
Constitutional (12.6%)	<0.0001	0.365	<0.0001	0.386
Lymphadenopathy (24.5%)	<0.0001	0.497	<0.0001	0.498
Glandular (25.2%)	<0.0001	0.323	<0.0001	0.311
Articular (57%)	<0.0001	0.393	<0.0001	0.454
Cutaneous (13.1%)	<0.0001	0.354	<0.0001	0.346
Pulmonary (6.5%)	<0.0001	0.276	<0.0001	0.262
Renal (2.8%)	<0.0001	0.183	<0.0001	0.193
Muscular (1%)	0.031	0.069	0.014	0.079
PNS (5.7%)	<0.0001	0.285	<0.0001	0.291
CNS (1.4%)	0.0004	0.125	<0.0001	0.136
Haematological (25.5%)	<0.0001	0.391	<0.0001	0.351
Biological (53%)	<0.0001	0.327	<0.0001	0.225

PNS: peripheral nervous system; CNS: central nervous system.

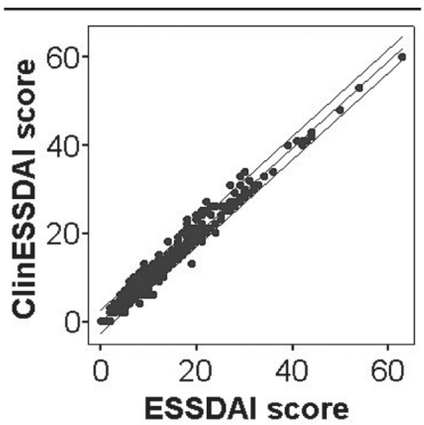

Fig. 1. Correlation between ESSDAI and ClinESSDAI scores.

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Competing interests : none declared.

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