A new score for assessment of lupus disease activity: presentation, validation and application

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Introduction Systemic Lupus Erythematosus (SLE), also known simply as Lupus, is an autoimmune disease that presents a great variety of clinical and serological manifestations. A patient with lupus may present periods of illness, called flares, alternating with periods of remission, during which there are few symptoms. Stability of the patient is fundamental requiring a correct evaluation of the disease activity to define the therapeutics to be adopted, as well as to monitor its effectiveness.

Over the last three decades, multiple disease activity indices have been developed, weighting differently clinical and laboratory manifestations. The SLE Disease Activity Index (SLEDAI-2k) is the most widely used SLE disease activity measure[1-3], being taken as a reference in clinical trials. Jesus et al. [4] have shown that the performance of SLEDAI-2k in detecting clinically meaningful changes in disease activity is limited, which has important implications in daily clinical practice, and in assessing the efficacy of new medications in clinical trials.

This presentation summarizes the work developed to derive and validate a new index to measure SLE activity. This new index is called SLE Disease Activity Score (SLE-DAS). The development of the SLE-DAS is presented and its ability to detect changes in the patient's clinical status is assessed through internal and external validation.

Methods The development of the new index involved 315 patients, followed between January 2014 and December 2017 at Lupus Clinic at Rheumatology Department, Centro Hospitalar e Universitário de Coimbra (CHUC), Portugal. Clinical and laboratory data on disease activity were collected at each visit of the follow-up, the SLEDAI-2k index was calculated and the Physician Global Assessment (PGA) was recorded (the PGA is a score assigned by an experienced physician to reflect the activity of the disease).

For each patient, data from the visit with the highest disease activity during follow-up was selected. Through multiple regression, with PGA as dependent variable, a model to predict disease activity based on clinical and laboratory data was derived. Rare manifestations in lupus were not included in the regression model due to lack of data and were added to the model weighted according to the clinical experience of experts with extensive knowledge in SLE.

The internal validation of SLE-DAS was carried out using multiple visit records during follow-up. Spearman correlations between PGA and both SLE-DAS and SLEDAI-2K were calculated. Higher correlations were obtained for SLE-DAS.

Receiver Operating Characteristic curves (ROC curves) were used to find an ideal cut-off value for SLE-DAS variation to identify a clinically meaningful change in disease activity (variation in SLE-DAS≥1.72 points). SLE-DAS was shown to have a better discriminative ability when compared to SLEDAI-2k: the area under the ROC curves (AUC) were compared through

DeLong's test. McNemar's test was used to assess whether there was a significant difference between the SLE-DAS and SLEDAI-2K sensitivity and specificity for clinically meaningful changes.
External validation was performed with data of 196 patients followed at Rheumatology Unit, University of Padova, Italy. The SLEDAI-2k and SLE-DAS indices were calculated with the records of the last follow-up visit. The SLE-DAS was calculated using the model proposed.
Considering the last two assessments in the follow-up period, patients with clinically meaningful worsening or improvement were identified. SLEDAI-2k and SLE-DAS were both calculated for these two visits and the variation of these two indices was determined. This information was used to assess SLE-DAS's ability to detect a clinically meaningful improvement and a clinically meaningful worsening.
Results As in the internal validation, in the external validation cohort a higher correlation between the PGA value and SLE-DAS was observed, compared to the correlation between SLEDAI-2k and PGA (r_s=0.875, p<0.0005 vs r_s=0.839, p<0.0005). In addition, resorting to beta regression coefficients, SLE-DAS revealed higher relative importance in the determination of PGA than SLEDAI-2k.
The variation in SLE-DAS (change≥1.72 points) produced an AUC greater than that of SLEDAI-2k (change ≥4) in terms of detecting clinically relevant changes in the patient's condition (AUC´s for improvement: 0.938 vs 0.807, p=0.005; for worsening: 0.998 vs 0.928, p=0.032). SLE-DAS showed a higher sensitivity than SLEDAI-2K to detect a clinically meaningful improvement (89.5% vs 47.4%, p=0.008) and higher sensitivity for clinically meaningful worsening (95.5% vs 59.1%, p=0.008), while maintaining similar specificities.
Discussion and conclusions: SLE-DAS is a "friendly" score, easy to apply: an online SLE-DAS calculator has been developed, in which the physician indicates the patient´s clinical and laboratorial manifestations and the value of SLE-DAS is determined (available at http://sle-das.eu). SLE-DAS is, therefore, an easy alternative to the current SLEDAI-2k index. SLE-DAS performs much better than SLEDAI-2K in terms of sensitivity to detect a clinically meaningful change, while presenting a high specificity. Such a performance can have major implications in the interpretation of clinical trials applying the disease activity as the primary endpoint, and in daily clinical practice, where SLE-DAS could provide robust guidance for treatment in the individual patient. As future work we intend to define cutoff values for the SLE remission state.

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