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# Systemic Lupus Erythematosus Disease Activity Index 2000

DAFNA D. GLADMAN, DOMINIQUE IBAÑEZ, and MURRAY B. UROWITZ

**ABSTRACT. Objective.** To describe the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), a modification of SLEDAI to reflect persistent, active disease in those descriptors that had previously only considered new or recurrent occurrences, and to validate SLEDAI-2K against the original SLEDAI as a predictor for mortality and as a measure of global disease activity in the clinic.

**Methods.** All visits in our cohort of 960 patients were used to correlate SLEDAI-2K against the original SLEDAI, and the whole cohort was used to validate SLEDAI-2K as a predictor of mortality. A subgroup of 212 patients with SLE followed at the Lupus Clinic who had 5 regular visits, 3–6 months apart, in 1991–93 was also included. An uninvolved clinician evaluated each patient record and assigned a clinical activity level. The SLEDAI score was calculated from the database according to both the original and modified definitions.

**Results.** SLEDAI-2K correlated highly ( $r = 0.97$ ) with SLEDAI. Both methods for SLEDAI scoring predicted mortality equally ( $p = 0.0001$ ), and described similarly the range of disease activity as recognized by the clinician.

**Conclusion.** SLEDAI-2K, which allows for persistent activity in rash, mucous membranes, alopecia, and proteinuria, is suitable for use in clinical trials and studies of prognosis in SLE. (*J Rheumatol* 2002;29:288–91)

## Key Indexing Terms:

SYSTEMIC LUPUS ERYTHEMATOSUS    DISEASE ACTIVITY    SLEDAI    OUTCOME

The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was developed and validated as a clinical index for the measurement of disease activity in SLE and has been used as a global measure of disease activity in SLE since its introduction in 1985<sup>1,2</sup>. This index was modeled on clinicians' global judgment. It was developed with a panel of experienced rheumatologists with expertise in SLE, using well established group techniques and index development methodology. The index has been used successfully by both expert clinicians<sup>3</sup> and trainees<sup>4</sup>, and has been shown to be valuable in both research and clinical settings<sup>5,6</sup>. It has also been shown to be time sensitive<sup>7</sup>.

The variables proteinuria, rash, alopecia, and mucous membrane lesions are counted as active in the SLEDAI only at their first occurrence, or upon recurrence. This was done to distinguish active from chronic lesions, the latter more likely to represent damage.

Intuitively, physicians would prefer to use these descriptors as active any time they are present. Indeed the SELINA trial group modified the SLEDAI to insure that the descriptors of organ system involvement reflected ongoing disease activity<sup>8</sup>.

However, this group made other modifications to the SLEDAI such as adding scleritis and episcleritis as descriptors of active disease with high activity weighting of 8. These manipulations were made without validation of the new index with the same rigorous methodological approach as the derivation of the original index, nor did they validate this index against the original SLEDAI.

Our aims were: (1) to describe SLEDAI 2000 (SLEDAI-2K), a modification of SLEDAI to reflect persistent, active disease in those descriptors that had previously only considered new or recurrent occurrences; and (2) to validate SLEDAI-2K against the original SLEDAI, (a) as a predictor for mortality and (b) as a measure of global disease activity in the clinic.

## MATERIALS AND METHODS

*University of Toronto Lupus Clinic.* All visits for patients registered in our cohort were included to compare the scores calculated for the original SLEDAI and SLEDAI-2K. The whole cohort was also used to validate the SLEDAI-2K against the original SLEDAI at presentation as a predictor of mortality (Table 1).

Table 1. Characteristics of total cohort.

Patients (n)	960
Female/male (%)	842 (87.7)/118 (12.3)
Alive/dead (%)	792 (82.5)/168 (17.5)
Race: Caucasian/Black/other (%)	778 (81.5)/71 (7.48)/106 (11.0)
Age at diagnosis, yrs	32.9 (13.68) [8–83]*
Age at first visit, yrs	36.3 (13.60) [10–84]*
Assessments (n)	18,636
Mean assessments per patient	19.2 (19.8) [1–106]*
Duration of followup, yrs	8.2 (7.4) [0–30.5]*

\*Mean (SD) [range].

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Table 2. SLEDAI- 2K data collection form.

Study No.: \_\_\_\_\_ Patient Name: \_\_\_\_\_ Visit Date: \_\_\_\_\_

(Enter weight in SLEDAI Score column if descriptor is present at the time of the visit or in the preceding 10 days.)

Weight	SLEDAI SCORE	Descriptor	Definition
8	_____	Seizure	Recent onset, exclude metabolic, infectious or drug causes.
8	_____	Psychosis	Altered ability to function in normal activity due to severe disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Exclude uremia and drug causes.
8	_____	Organic brain syndrome	Altered mental function with impaired orientation, memory, or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious, or drug causes.
8	_____	Visual disturbance	Retinal changes of SLE. Include cytoid bodies, retinal hemorrhages, serous exudate or hemorrhages in the choroid, or optic neuritis. Exclude hypertension, infection, or drug causes.
8	_____	Cranial nerve disorder	New onset of sensory or motor neuropathy involving cranial nerves.
8	_____	Lupus headache	Severe, persistent headache; may be migrainous, but must be nonresponsive to narcotic analgesia.
8	_____	CVA	New onset of cerebrovascular accident(s). Exclude arteriosclerosis.
8	_____	Vasculitis	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, or biopsy or angiogram proof of vasculitis.
4	_____	Arthritis	≥ 2 joints with pain and signs of inflammation (i.e., tenderness, swelling or effusion).
4	_____	Myositis	Proximal muscle aching/weakness, associated with elevated creatine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis.
4	_____	Urinary casts	Heme-granular or red blood cell casts.
4	_____	Hematuria	>5 red blood cells/high power field. Exclude stone, infection or other cause.
4	_____	Proteinuria	>0.5 gram/24 hours
4	_____	Pyuria	>5 white blood cells/high power field. Exclude infection.
2	_____	Rash	Inflammatory type rash.
2	_____	Alopecia	Abnormal, patchy or diffuse loss of hair.
2	_____	Mucosal ulcers	Oral or nasal ulcerations.
2	_____	Pleurisy	Pleuritic chest pain with pleural rub or effusion, or pleural thickening.
2	_____	Pericarditis	Pericardial pain with at least 1 of the following: rub, effusion, or electrocardiogram or echocardiogram confirmation.
2	_____	Low complement	Decrease in CH50, C3, or C4 below the lower limit of normal for testing laboratory
2	_____	Increased DNA binding	Increased DNA binding by Farr assay above normal range for testing laboratory.
1	_____	Fever	>38° C. Exclude infectious cause.
1	_____	Thrombocytopenia	<100,000 platelets / x10 <sup>9</sup> /L, exclude drug causes.
1	_____	Leukopenia	< 3,000 white blood cells / x10 <sup>9</sup> /L, exclude drug causes.

**TOTAL SLEDAI SCORE** \_\_\_\_\_

As of December 2000 there were 960 patients registered in the cohort, of whom 168 have died. All deaths are recorded according to a standardized form in the database, and we have only a 10% lost to followup rate and can account for the vast majority of deaths<sup>9</sup>. We have previously shown that SLEDAI at presentation predicts mortality. The survival analysis was repeated using the original SLEDAI and SLEDAI-2K in the entire cohort.

To test the validity of the modified index in describing changes in global disease activity in our clinic, we used patients who attended the clinic in 1992

and who had 5 consecutive regular visits between 1991 and 1993. A clinician who did not know the patients and was blind to their SLEDAI score evaluated each patient record and assigned a clinical activity score for each assessment according to the following scale: 0 = no activity; 1 = mild activity with no therapeutic intervention; 2 = activity, but improvement from previous visit; 3 = persistent activity/refractory to treatment; 4 = flare, defined as one of the following: the introduction of new treatment in the presence of worsening of an already active system or in response to the activation of a new system; an

increase in medication dosage for the above reasons; indication of concern in the physician's notes (arrangement for an earlier appointment for the assessment of SLE disease activity or investigation related to SLE including measurement of anti-DNA antibodies and serum complement levels, and 24 hour urine protein determination); the use of the term flare in the physician's notes (i.e., treating physician's impression of increased disease activity); new diagnosis of SLE.

**Modification of SLEDAI (SLEDAI-2K).** The original SLEDAI was used as described<sup>1,2</sup>. Among the SLEDAI descriptors, alopecia, mucous membrane lesions, and rash had been scored only if they were new or recurrent, and in the case of proteinuria if there was new onset or a recent increase of more than 0.5 g/24 h. We modified the definition of these descriptors to include the presence of any rash, alopecia, or mucosal ulcers and new, recurrent, or persistent proteinuria > 0.5 g/24 h (Table 2).

**Statistical analysis.** Descriptive statistics were calculated for the characteristics of both cohorts. T tests were used to compare mean SLEDAI and SLEDAI-2K across mortality. They were also used to compare the mean change in SLEDAI to the mean change in SLEDAI-2K for each level of subjective categories. Linear regression was used to test for trend in change in SLEDAI and in SLEDAI-2K across the subjective categories.

## RESULTS

**SLEDAI-2K compared to SLEDAI in the entire cohort.** SLEDAI calculations in the entire cohort were available for 18,636 visits. SLEDAI and SLEDAI-2K were the same in 14,532 visits (78%). In the remaining 4104 visits the differences were due to proteinuria in 1355 (7.3% of all visits), rash: 1378 (7.4%), alopecia: 1116 (6.0%), and mucous membrane ulcers: 752 (4.0%) (more than one item was different in some visits). The average magnitude of change when present was 2.91, with SLEDAI-2K being greater than SLEDAI. The correlation between SLEDAI-2K and SLEDAI across all visits was  $r = 0.97$  ( $p = 0.0001$ ).

**SLEDAI-2K compared to SLEDAI at presentation as a predictor for mortality.** At presentation the mean (SD) SLEDAI for the whole group was 10.2 (8.6), ranging from 0 to 56. The mean (SD) SLEDAI-2K was 10.4 (8.7) with a similar range. Both the original SLEDAI and SLEDAI-2K at presentation were equally significant predictors for all-cause mortality in our entire cohort (Table 3).

**SLEDAI-2K compared to SLEDAI as a measure of global disease activity in the clinic.** Two hundred twelve patients seen in 1992 had 5 regular visits, 3–6 months apart, between 1991 and 1993. There were 191 women and 21 men, with a mean age of 41 years at the time of the study, and a mean disease duration of 10 years. The majority of the patients were Caucasian (76.9%). Table 4 lists the characteristics of this patient cohort.

SLEDAI-2K describes a similar progression over a range of disease activity and of the same magnitude as SLEDAI

Table 4. Characteristics of SLE patients used in the evaluation of disease activity.

Patients (n)	212
Female/Male (%)	191 (90.1)/21 (9.9)
Race: Caucasian/Black/other (%)	163 (76.9)/23 (10.8)/26 (12.3)
Age at diagnosis, yrs	31.0 (13.5) [8–75]*
Age at first visit, yrs	33.9 (12.7) [16–75]*
Age at study, yrs	41.2 (12.7) [19–75]*
Disease duration at first visit, yrs	2.9 (4.6) [0–25]*
Disease duration at study, yrs	10.2 (7.6) [0–41]*
Assessments during study (n)	1060
Length of followup during study, mo	15.5 (5.0) [4–27]*
SLEDAI at first visit to clinic	10.2 (8.3) [0–55]*
SLEDAI-2K at first visit to clinic	10.3 (8.3) [0–55]*

\* Mean (SD) [range].

(Table 5). As expected, SLEDAI-2K scores were minimally higher at a number of levels, reflecting the 4 modified variables (rash, alopecia, mucous membrane ulcers, and proteinuria). A regression model for SLEDAI and SLEDAI-2K between the activity categories indicates that the scores of the individual categories are significantly different ( $p = 0.0001$ ). Median SLEDAI and SLEDAI-2K values for the activity levels were similar (Table 5). The change from the previous visit in SLEDAI and SLEDAI-2K over the range of disease activity level was also very similar (Table 6). Linear regressions revealed that all levels of disease activity were different for both SLEDAI and SLEDAI-2K. SLEDAI-2K thus reflects the change in disease activity as reported for SLEDAI<sup>10</sup>.

## DISCUSSION

In the derivation of the SLEDAI, investigators were focused on describing pure disease activity as opposed to damage from disease or therapy. Therefore, in the glossary of the original SLEDAI, items were not scored as active if they could represent chronicity or damage. With wider use clinicians have interpreted chronic active lesions in the skin, hair, and mucous membranes or persistent proteinuria as equivalent to active lesions. Furthermore, in clinical trials if these lesions persisted and were not scored as active, this would cause an erroneous interpretation of improvement related to the therapy under investigation. This led the investigators in the SELENA trial to modify some aspects of the SLEDAI, but without any validation of their modification. For that reason we set out to modify the SLEDAI to include persistent disease activity in the features noted above, and to validate the modification.

We propose modifications to the SLEDAI such that persistent active disease in the items alopecia, mucous membrane ulcers, rash, and proteinuria would be scored. The revised SLEDAI will be identified as SLEDAI-2K to differentiate it from the original index. We validated SLEDAI-2K against the original SLEDAI in 18,636 patient visits in our Lupus Clinic and found that the score was different in only 4104 instances (22%). SLEDAI-2K is comparable to the original SLEDAI as a predictor of mortality. SLEDAI-2K describes disease activ-

Table 3. Correlation of SLEDAI and SLEDAI-2K with mortality in 960 patients with SLE at presentation. Data are mean (SD).

Instrument	Alive, n = 792	Dead, n = 168	p
SLEDAI	9.44 (7.88)	13.95 (10.76)	0.0001
SLEDAI-2K	9.69 (7.93)	14.01 (10.80)	0.0001

Table 5. SLEDAI, SLEDAI-2K, and clinical activity levels in 1060 assessments.

Activity Level	No. (%)	SLEDAI*	SLEDAI-2K*	p
0–No activity	465 (43.9)	1.95 (2.29) [2]	2.23 (2.34) [2]	0.066
1–Mild activity	231 (21.8)	3.80 (2.85) [4]	4.42 (2.93) [4]	0.023
2–Activity, but improvement	87 (8.2)	6.74 (3.93) [6]	7.45 (3.93) [8]	0.233
3–Persistent activity	165 (15.6)	7.78 (4.05) [8]	8.80 (4.05) [8]	0.023
4–Flare	112 (10.6)	9.37 (6.13) [9]	9.76 (6.15) [9]	0.632

\*Mean score (SD) [median].

Table 6. Change ( $\Delta$ ) in SLEDAI and SLEDAI-2K by activity levels.

Activity Level	N	$\Delta$ SLEDAI*	$\Delta$ SLEDAI-2K	p
0–No activity	380	–0.71 (3.30)	–0.75 (3.27)	0.860
1–Mild activity	178	–0.87 (4.02)	–0.78 (4.10)	0.835
2–Activity, but improvement	76	–2.59 (5.03)	–2.57 (4.96)	0.974
3–Persistent activity	125	–0.52 (3.96)	–0.23 (3.77)	0.556
4–Flare	89	4.48 (5.21)	4.57 (5.11)	0.908

\* Mean score (SD).

ity at various activity levels in a comparable manner to the original SLEDAI. SLEDAI-2K is equivalent to SLEDAI in describing changes in disease activity from one visit to the next.

Therefore, SLEDAI-2K, which allows for persistent activity in rash, mucous membrane ulcers, alopecia, and proteinuria, is suitable for use in clinical trials and studies of prognosis in SLE. We recommend the use of the modified SLEDAI, SLEDAI-2K, for the assessment of global disease activity in SLE.

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