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THE RELIABILITY OF THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS/AMERICAN COLLEGE OF RHEUMATOLOGY DAMAGE INDEX IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

DAFNA D. GLADMAN, MURRAY B. UROWITZ, CHARLES H. GOLDSMITH, PAUL FORTIN, ELLEN GINZLER, CAROLINE GORDON, JOHN G. HANLY, DAVID A. ISENBERG, KENNETH KALUNIAN, OLA NIVED, MICHELLE PETRI, JORGE SANCHEZ-GUERRERO, MICHAEL SNAITH, and GUNNAR STURFELT

Objective. **To test the reliability of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index and the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) in the assessment of patients with SLE.**

Methods. **Ten patients with SLE, representing a spectrum of damage and activity, were included. Each patient was examined by 6 of 10 physicians from 5 countries, representing 10 lupus clinics. The SLICC/ACR Damage Index was used to assess accumulated damage, and the SLEDAI was used to assess disease activity. The order of the patients and physicians was randomized according to a Youden square design.**

Results. **The SLICC/ACR Damage Index detected differences among patients ($P < 0.001$). There was no detectable observer difference ($P = 0.933$), and there was no order effect ($P = 0.261$). Similar results were obtained with the SLEDAI. There was concordance in the SLICC/ACR Damage Index among observers, despite a wide spectrum of disease activity detected by the SLEDAI.**

Conclusion. **Physicians from different centers are able to assess patients with SLE in a reproducible way, using the SLEDAI to assess disease activity and the SLICC/ACR Damage Index to assess accumulated damage.**

Systemic lupus erythematosus (SLE) is a multisystem disease with a variable course and prognosis. It has become clear that to assess patients with SLE appropriately, appraisal of both disease activity and accumulated damage is required. A number of instruments have been developed and validated to describe disease activity in an individual patient during a clinic visit (1). One such instrument is the SLE Disease Activity Index (SLEDAI), which was developed during a conference on prognosis of SLE in 1985 (2). This instrument was developed and initially validated by a group of investigators from 10 North American centers (2), and was further shown to be reliable by both experienced (3,4) and nonexperienced observers (5). The SLEDAI was further shown to be sensitive to changes in disease activity over time (6).

From the Systemic Lupus International Collaborating Clinics (SLICC) and the American College of Rheumatology Diagnostic and Therapeutic Criteria Subcommittee.

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Dafna D. Gladman, MD, FRCPC, Murray B. Urowitz, MD, FRCPC: The Centre for Prognosis Studies in the Rheumatic Diseases, The Toronto Hospital, Toronto, Ontario, Canada; Charles H. Goldsmith, PhD: McMaster University, Hamilton, Ontario, Canada; Paul Fortin, MD, MPH: Montreal General Hospital, Montreal, Quebec, Canada; Ellen Ginzler, MD, MPH: State University of New York Health Science Center at Brooklyn; Caroline Gordon, MD: Medical School, Birmingham University, Birmingham, UK; John G. Hanly, MD, FRCPC: Dalhousie University, Halifax, Nova Scotia, Canada; David A. Isenberg, MD, MRCP: University College, and Middlesex Hospital Medical School, London, UK; Kenneth Kalunian, MD: University of California, Los Angeles; Ola Nived, MD, PhD, Gunnar Sturfelt, MD: University Hospital, Lund, Sweden; Michelle Petri, MD, MPH: Johns Hopkins Medical School, Baltimore, Maryland; Jorge Sanchez-Guerrero, MD: Instituto Nacional Nutrición Salvador Zubirán, Vasco de Quiroga, Mexico; Michael Snaith, MD, FRCP: Institute for Bone and Joint Medicine, University of Sheffield, Sheffield, UK.

Address reprint requests to Dafna D. Gladman, MD, FRCPC, Centre for Prognosis Studies, The Toronto Hospital, Western Division, 399 Bathurst Street, 1-318, Toronto, Ontario M5T 2S8, Canada.

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The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index for SLE was developed by the SLICC and was accepted by the ACR as a validated measure of damage for SLE (7). This instrument measures accumulated organ damage that has occurred since the onset of SLE, resulting from either the disease process or its sequelae. It includes descriptors in 12 organ systems. The SLICC/ACR Damage Index has been demonstrated to have construct validity (7). To further verify the Damage Index, it was considered necessary to determine its reliability by comparing its use during actual patient assessments. The relationship of disease activity scores to damage index scores is not clear.

The aims of this investigation were 1) to test the reliability of the SLICC/ACR Damage Index in the assessment of live patients with SLE; and 2) to correlate damage index scores with disease activity scores (using the SLEDAI) in the same patients.

PATIENTS AND METHODS

Patient selection. Ten patients were recruited from among SLE patients attending the University of Toronto Lupus Clinic at the Wellesley Hospital. Patients were selected by the host investigators to represent a spectrum of disease activity and damage. All patients fulfilled at least 4 of the 1982 revised ACR criteria for the classification of SLE (8).

Observers. Ten physicians, who were members of the SLICC and represented 10 different lupus clinics from 5 countries, participated in the study.

Assessment of damage. The SLICC/ACR Damage Index was used to record damage accumulated in these patients. This instrument was developed by members of the SLICC and has been shown to be valid for the assessment of damage (7). Three items were added to the original instrument (Appendix 1): 1) in the pulmonary system, lung resection, not for malignancy, was added as an alternative to pulmonary infarction; 2) pancreatic insufficiency requiring enzyme replacement was added to the gastrointestinal system; and 3) ruptured tendons was added to the musculoskeletal system.

Assessment of disease activity. The SLEDAI was used to measure disease activity at the time of the study. This is a validated instrument that has previously been shown to be reproducible (2–5).

Study design. Each patient was assessed by 6 physicians, since it was believed that the patients would not tolerate more than 6 evaluations within the day of the study. The order of patients and physicians was randomized according to a Youden square design. This method allows an improved experimental design, provides for examinations during a fixed period of time, and includes specific numbers of observers and patients. This design controls 2 different sources of variability that may account for the 3 experimental variations: observer variability, order of examinations, and patient effects (9,10). It allows for the testing of observer, order, and patient effects. Each physician completed an assessment of disease activity using the SLEDAI scoring system (2), as well as an assessment of damage using the SLICC/ACR Damage Index, for 6 patients (7). For each patient, the clinical chart was available for the physicians to identify previous damage.

Statistical analysis. Data were collected on scoring sheets and immediately entered in a computer. All statistical analyses were conducted with Minitab, version 7.2 (11). The data were analyzed with a 3-factor analysis of variance, with a 5% level of significance. Although not all of the 10 patients were assessed by the 10 observers, this analysis permitted the separate estimation of the patient, order, and observer factors using the general linear model command in Minitab. The SLICC/ACR Damage Index was compared with the SLEDAI using a product moment correlation coefficient.

Table 1. Demographic characteristics of the study patients*

Characteristic	
No. of patients	10
Female/male, no.	7/3
Mean age, years (range)	53.8 (27.9–71)
Mean disease duration, years (range)	18 (6–36)
Mean SLEDAI (range)	5.7 (0–16)
Mean SLICC/ACR DI (range)	4.7 (0–8)

* SLEDAI = Systemic Lupus Erythematosus Disease Activity Index; SLICC/ACR DI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

RESULTS

Ten patients participated in the study. There were 7 women and 3 men, with a mean age of 53.8 years and a mean disease duration of SLE of 18 years. The demographic characteristics for these patients are summarized in Table 1. Their cumulative disease manifestations and therapy are summarized in Table 2.

Analysis of variance for the SLICC/ACR Damage Index revealed that the Damage Index detected differences among patients ($P < 0.001$). The analysis further revealed that the SLICC/ACR Damage Index did not differ by physician (observer effect $P = 0.933$), nor did the order in which the physician saw the patients differ (order effect $P = 0.261$) (Table 3). Analysis of variance for the SLEDAI revealed that it was able to detect differences among patients ($P < 0.001$), while no observer or order effects were detected ($P = 0.467$ and $P = 0.498$, respectively) (Table 3).

No correlation was demonstrated between the SLICC/ACR Damage Index scores and the SLEDAI scores, with a correlation coefficient of 0.05.

Table 2. SLE manifestations and treatment throughout the disease course of the study patients*

Patient/sex/age	Disease duration, years	Lupus manifestations at any time	Therapies used
1/F/50	15.5	Arthritis, CNS, constitutional, DVT, endocarditis, GI, hypertension, infection, lymphadenopathy, mucous membrane, Raynaud's, renal, Sjögren's, skin, vasculitis	Steroids, chloroquine
2/F/57	22.5	Arthritis, cataracts, CNS, constitutional, hypertension, infection, pleurisy, renal, Raynaud's, vasculitis	Steroids, chloroquine, azathioprine
3/F/62	28.5	Angina, arthritis, CNS, constitutional, GI, hypertension, MI, mucous membrane, myositis, PE, pericarditis, renal, Sjögren's, skin, Raynaud's, thrombophlebitis	Steroids, chloroquine, azathioprine
4/M/71	14.5	Arthritis, CNS, constitutional, DVT, hypertension, infection, mucous membrane, pleurisy, Raynaud's, renal, Sjögren's, skin, splenomegaly, vasculitis	Steroids, chloroquine
5/F/62	36.5	Arthritis, CNS, constitutional, cytoid bodies, endocarditis, GI, infections, hypertension, lung, mucous membrane, renal, skin	Steroids, chloroquine, azathioprine
6/F/28	6.0	Arthritis, CNS, constitutional, GI, hypertension, infection, lung, mucous membrane, pleurisy, Raynaud's, renal, Sjögren's, skin	Steroids, chloroquine, azathioprine, methotrexate, cyclophosphamide
7/M/54	11.5	Angina, arthritis, cataracts, CNS, constitutional, GI, hepatomegaly, hypertension, lung, lymphadenopathy, MI, mucous membrane, Raynaud's, renal, skin, vasculitis	Steroids, chloroquine, azathioprine
8/F/59	9.5	Arthritis, cataracts, CNS, constitutional, diabetes, GI, hypertension, infections, mucous membrane, Sjögren's, Raynaud's, pancreatitis, pericarditis, renal, skin, vasculitis	Steroids, chloroquine, cyclosporin A
9/M/62	20.5	Arthritis, CNS, constitutional, DVT, lung, lymphadenopathy, pericarditis, pleurisy	Steroids
10/F/34	15.5	Arthritis, CNS, constitutional, GI, infection, lymphadenopathy, lung, pericarditis, PE, Raynaud's, renal, thrombophlebitis, vasculitis	Steroids, chloroquine, azathioprine

* SLE = systemic lupus erythematosus; CNS = central nervous system; DVT = deep venous thrombosis; GI = gastrointestinal; MI = myocardial infarction; PE = pulmonary embolus.

DISCUSSION

The SLICC/ACR Damage Index was shown to have content and face validity when it was developed by members of the SLICC (7). Members of the SLICC have also demonstrated their ability to record SLICC scores similarly, based on case scenarios. The purpose of the current investigation was to test its interassessor reliability in the assessment of live patients with SLE. The patients selected represented a spectrum of disease activity and damage, as outlined in Table 2. The design of this study allowed us to test patient, observer, and order effects simultaneously. The study demonstrated the reproducibility of the SLICC/ACR Damage Index. While the instrument was able to detect differences among patients, there were no detectable observer or order effects. Mean indices among the 10 physicians varied from a low of 3.00 to a high of 5.83. This extreme difference of 2.83 among physicians was not detectable with our design, since $P = 0.933$ as shown in Table 3. In this Youden square design, the differences among physicians were partially confounded by the patient differences, although the P value was adjusted for the patient differences. The SLICC group has not decided what would be a clinically important difference for the Dam-

Table 3. Analysis of variance results*

Source	SLICC/ACR Damage Index			SLEDAI		
	Degrees of freedom	F	P	Degrees of freedom	F	P
Patient	9	22.83	<0.001	9	16.88	<0.001
Physician	9	0.39	0.933	9	0.99	0.467
Order	5	1.36	0.261	5	0.89	0.498
Error	36	–	–	–	–	–
Total	59	–	–	–	–	–

* See Table 1 for definitions.

age Index. Using various values for clinically important differences, sample size calculations revealed that our study had an 80% power to detect an extreme difference of ~2.4, slightly smaller than the value of 2.83 that we saw.

This study thus provides evidence that physicians from different centers and different health care systems are able to record accumulated damage in a particular patient in a similar way. This information is useful for collaborative studies of patients with SLE that include the assessment of damage.

The assessment of disease activity in these patients was performed to determine whether the extent of activity would influence the assessment of damage. Although the reproducibility of the SLEDAI has previously been demonstrated (3), we wanted to confirm that it was reliable in this study as well. The study demonstrated that there was no order effect, and no detectable effect was introduced by the multiple examinations either for the SLICC/ACR Damage Index or for the SLEDAI. Thus, the observers scored the Damage Index in a similar manner, despite differences in disease activity among these patients.

This study clearly demonstrates that at one point in time, there is no relationship between the disease activity score and the accumulated damage score. Similar results have been previously demonstrated from other centers (12–14), but this was done by members of the individual center. We now confirm the lack of correlation between disease activity and damage at one point, with a study involving clinicians from different countries. Physicians from different centers are clearly able to assess patients with SLE in a reproducible way, using the SLEDAI to assess disease activity and the SLICC/ACR Damage Index to assess accumulated damage. The SLICC/ACR Damage Index can therefore be used in clinical research involving multiple centers, with standardization and training of assessors.

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APPENDIX 1: THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS/AMERICAN COLLEGE OF RHEUMATOLOGY DAMAGE INDEX

TOTAL SCORE _____

SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS

Patient Name:_____ **Study No.** _____

Assessment Date: ___/___/___

Damage occurring since diagnosis of lupus, ascertained by clinical assessment and present for at least 6 months unless otherwise stated. Repeat episodes mean at least 6 months apart to score 2. The same lesion cannot be scored twice.

ITEM	SCORE (circle)
OCULAR (Either eye, by clinical assessment)	
Any cataract ever	0 1
Retinal change OR Optic atrophy	0 1
NEUROPSYCHIATRIC	
Cognitive impairment (e.g. memory deficit, difficulty with calculation, poor concentration, difficulty in spoken or written language, impaired performance level)	
OR Major psychosis	0 1
Seizures requiring therapy for 6 months	0 1
Cerebral vascular accident ever (Score 2 if >1), resection not for malignancy	0 1 2
Cranial or peripheral neuropathy (excluding optic)	0 1
Transverse myelitis	0 1
RENAL	
Estimated or measured GFR <50%	0 1
Proteinuria 24 h, ≥ 3.5 g	0 1
OR	
End-stage renal disease (regardless of dialysis or transplantation)	3
PULMONARY	
Pulmonary hypertension (right ventricular prominence, or loud P2)	0 1
Pulmonary fibrosis (physical and X-ray)	0 1
Shrinking lung (X-ray)	0 1
Pleural fibrosis (X-ray)	0 1
Pulmonary infarction (X-ray) OR resection not for malignancy	0 1
CARDIOVASCULAR	
Angina OR coronary artery bypass	0 1
Myocardial infarction ever (Score 2 if >1)	0 1 2
Cardiomyopathy (ventricular dysfunction)	0 1
Valvular disease (diastolic murmur, or a systolic murmur > 3/6)	0 1
Pericarditis x 6 months or pericardiectomy	0 1
PERIPHERAL VASCULAR	
Claudication x 6 months	0 1
Minor tissue loss (pulp space)	0 1
Significant tissue loss ever (eg. loss of digit or limb, resection) (Score 2 if >1)	0 1 2
Venous thrombosis with swelling, ulceration, OR venous stasis	0 1
GASTROINTESTINAL	
Infarction or resection of bowel (below duodenum), spleen, liver or gall bladder ever (Score 2 if >1)	0 1 2
Mesenteric insufficiency	0 1
Chronic peritonitis	0 1
Stricture OR upper gastrointestinal tract surgery ever	0 1
Pancreatic insuffiency requiring enzyme replacement or with pseudocyst	0 1
MUSCULOSKELETAL	
Atrophy or weakness	0 1
Deforming or erosive arthritis (including reducible deformities, excluding avascular necrosis)	0 1
Osteoporosis with fracture or vertebral collapse (excluding avascular necrosis)	0 1
Avascular necrosis (Score 2 if >1)	0 1 2
Osteomyelitis	0 1
Ruptured tendons	0 1
SKIN	
Alopecia	0 1
Extensive scarring or panniculum other than scalp and pulp space	0 1
Skin ulceration (excluding thrombosis) for more than 6 months	0 1
PREMATURE GONADAL FAILURE	0 1
DIABETES (regardless of treatment)	0 1
MALIGNANCY (Exclude dysplasia)	0 1 2