High Predictive Value of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for Survival in Systemic Lupus Erythematosus

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ABSTRACT. ***Objective.*** We previously reported high Systemic Lupus International Collaborating Clinics (SLICC) scores in fatal cases of systemic lupus erythematosus (SLE) from our inception cohort. This study was done to clarify if the SLICC damage scores 5 years after diagnosis predicted the outcome.

Methods. We studied 80 patients with SLE (70 women, 10 men), all enrolled and diagnosed during the years 1981 through 1991 in our inception cohort, and all alive 5 years after inclusion into the cohort. In all patients the SLICC/American College of Rheumatology (ACR) damage index (DI) was scored at 5 years after SLE diagnosis, and these scores were tested for predictive value. The outcomes were survival or late mortality within the following median observation period of 7 years. All surviving patients were followed through 1999, and no patient was lost to followup.

Results. At study entry, 5 years after the diagnosis of SLE, 37 patients had no damage to score with SLICC. Of the remaining 43 patients, 25 had a score of 1 and 18 had a score of 2 or more. In total, 14 fatalities occurred within 7 years after study entry, 7 among the 18 with initial SLICC/ACR DI of 2 or more compared with 7 fatalities among the 62 with less or no damage ($p < 0.01$). Cardiovascular or cerebrovascular SLICC/ACR DI items were more common in fatal cases than in survivors ($p < 0.001$). A SLICC score at 5 years of 2 or more increased the relative risk for fatality by 3.4 (95% CI 1.5–14.4), and had a predictive value of 38%. A SLICC score of 0 at 5 years gave an odds ratio in favor of survival of 0.06 (95% CI 0.0–0.5) and had a predictive value for survival of 97%. During an extended followup for one more year the predictive value of damage for fatalities was even more pronounced ($p = 0.003$, log-rank).

Conclusion. SLICC damage scores registered 5 years after SLE diagnosis have a high predictive value for survival during the following median observation time of 7 years. These data provide strong evidence that the items included in the SLICC score are clinically relevant. (J Rheumatol 2002;29:1398–400)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS SURVIVAL MORTALITY
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The survival of patients with systemic lupus erythematosus (SLE) has improved over the last decades, and today 5 year survivals over 90% are reported from most centers worldwide[1]. The bimodal mortality pattern, first reported by Urowitz and coworkers, identified atherosclerotic organ damage as the most important cause of late mortality[2]. The late mortality has not decreased to the same extent as the early mortality in SLE. In agreement with this, in a recent series from our center, the 10 year survival was decreased compared to an age and sex matched healthy population[3].

The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (DI) for SLE was developed by the SLICC and was adopted by the ACR as a validated measure of damage for SLE[4]. This instrument measures accumulated organ damage that has occurred since the onset of SLE. It includes descriptors in 12 organ systems. In the series from our unit we reported high SLICC/ACR DI scores in the cases of fatal SLE from our epidemiologically based inception cohort[3], an observation also reported from other centers[5,6].

This study was done to analyze if the SLICC/ACR DI scores 5 years after diagnosis predicted the outcome in our

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cohort of SLE patients, especially survival and late mortality. The 5 year starting point was chosen since, in our experience, few patients accrue damage within the first years in this cohort with mild disease.

MATERIALS AND METHODS

Patients. All patients living within the Health Care District of Lund/Orup (mean adult population of 172,300) and diagnosed with SLE during the years 1981 through 1991 and being alive 5 years after diagnosis were included. The study group subsequently consisted of 80 Caucasian patients. The patients were retrieved through different sources, both local clinical diagnosis registries and laboratory registries. The completeness of retrieval has been confirmed with the capture–recapture technique[7]. All patients had a multisystemic disease and a clinical diagnosis of SLE, and 78 of the patients fulfilled 4 or more ACR classification criteria for SLE[8]. Two patients with a clinical diagnosis of SLE fulfilled only 3 ACR criteria: one was a 44-year-old woman with photosensitivity, serositis, fever episodes, tenosynovitis, migraine, and antinuclear antibody (ANA) positivity; the other was a 39-year-old woman with discoid lesions, photosensitivity, alopecia, arthralgia, tenosynovitis, depression, cognitive dysfunction, sclerodactyly, and ANA positivity. Ten patients were male and 70 female. The median age at diagnosis was 47 years and the mean age 50 years.

Methods. SLICC/ACR DI measures were available on all included patients, and the scores accumulated 5 years after the diagnosis of SLE were used for calculation of the predictive value of the index. The outcomes were survival or late mortality within a median observation period of 7 years, or 12 years (range 8–18 yrs) after diagnosis of SLE. All surviving patients were followed through 1998 with an extended life table followup through 1999 and no case was lost to followup. The Kaplan-Meier method was used for calculation of survival and the log-rank test, chi-square test, or Spearman rank test for statistical analysis (Statistica computer program).

RESULTS

At study entry, 5 years after SLE diagnosis, 37 patients had no damage (DI = 0), 25 patients had a DI score of 1, and 18 patients had a damage score more than 1. The median, mean, and range of DI in different age groups were comparable, but with a tendency to higher range of scores over the age of 40 years. There was no correlation between age groups and SLICC/ACR DI.

Fourteen patients died within 7 years after study entry. Seven of these were among the 18 patients with a SLICC/ACR DI score ≥ 2 at entry, compared with 7 fatalities among the 62 patients with less or no damage at study entry ($p < 0.01$). The relative risk for mortality with a DI of 2 or more is 3.4 (95% confidence interval 1.5–14.4) and the predictive value 38%. Vascular items in the SLICC/ACR DI (angina pectoris, myocardial infarction, cardiovascular incident) were more prevalent in the fatal cases. Thus, 11 of the 14 patients who died had vascular items compared to 12 of the 66 surviving patients ($p < 0.001$). Indeed 6 of the 11 patients with a vascular item died of myocardial infarction and 4 of cerebrovascular stroke.

Only one out of 37 patients without damage at study entry died during the 7 year observation period, compared with 13 dying of the 43 with damage recorded at entry ($p < 0.001$). This gives an odds ratio in favor of survival of 0.06 (95% CI 0.0–0.5) and a predictive value for survival of 97% with SLICC/ACR DI of zero at study entry. The cause of death in the patient without damage was a biliary tract carcinoma.

During the entire observation period, up to 18 years from diagnosis in some cases (mean 8 years, range 8–18 years), 18 patients died. More patients survived in the group with no or minimal damage (SLICC/ACR DI of 0 or 1) at study entry ($p = 0.003$; Figure 1). Indeed the survival of those patients up to 10 years after diagnosis follows the data for the age and sex matched population of the area (data not shown, but as described[3]).

DISCUSSION

The main finding in this study was that SLICC/ACR Damage Index findings 5 years after diagnosis of SLE had good predictive value for both survival and mortality during a median of 7 years' followup. The strength of the study design is that this inception cohort includes all cases diagnosed in a defined geographical area during the years 1981 through 1991 and no cases were lost to followup. The drawback of the study is the rather low number of patients with SLE in the cohort.

Despite the comprehensive cohort under study, with many mild cases, and the improved survival for SLE in general the SLICC/ACR Damage Index plainly, even in this setting, conveys important predictive clinical information on prognosis. The late mortality in SLE, first described by Urowitz, *et al*[2] and confirmed in our own study[3], with fatalities caused mainly by cardiovascular manifestations, is today a major challenge for clinicians treating SLE.

Our observation of high SLICC/ACR DI scores in fatal cases is also reported by others. When members of the SLICC group followed 1297 patients with SLE for 10 years, those 99 who died had higher SLICC/ACR DI scores[5], and the same was true in a Danish inception cohort[6].

Our findings are in some ways parallel with the results in a very recent publication from the Toronto group. In that study SLICC/ACR DI with a score of 1 or more recorded at the initial assessment, within one year of SLE diagnosis, is associated with a higher rate of mortality. By contrast to our study showing high cardiovascular mortality, the mortality in the Toronto series was mostly renal[9]. In our inception cohort too few patients had developed any damage at one year to allow statistical analysis, perhaps due to the comprehensiveness of our cohort with many mild cases. Nevertheless, the conclusions regarding the predictive value of a SLICC registration after 5 years in our study and after one year in the Toronto study are in agreement.

The availability of an instrument of prognostic value will be helpful when stratifying future therapy studies to reduce the influence of atherosclerosis in SLE.

The SLICC/ACR DI has been extensively validated. It has been shown that physicians from different centers are able to assess patients with SLE in a reproducible way[10]; the

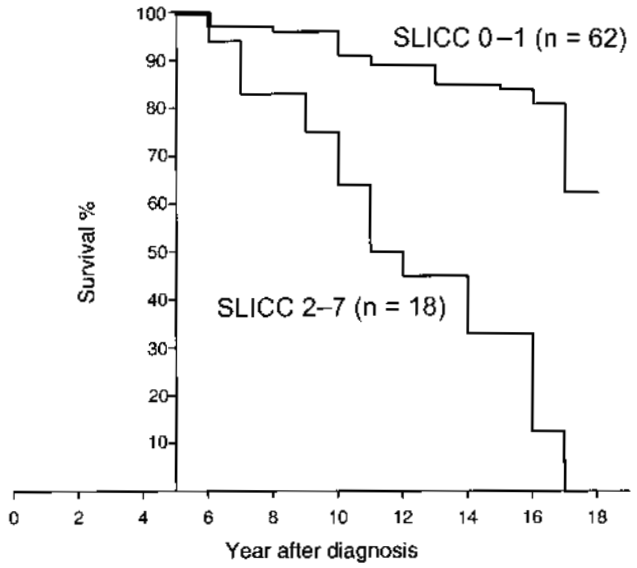

Figure 1. Survival in SLE based on presence or absence of SLICC/ACR damage scores of 2 or more, 5 years after SLE diagnosis (Kaplan-Meier).

accuracy of the medical record scoring of the index has been confirmed[11]; and based on the validation, the SLICC/ACR DI has been recommended for inclusion in clinical trials in SLE[12].

Damage is only one dimension to measure in clinical trials: the other 2, disease activity and health status, were shown to be important independent outcome variables[13]. More recent publications have shown that non-Caucasian race[14,15], longer disease duration[15-17], higher disease activity[15] and lower level of education all were associated with more organ damage[15]. It has also been shown that health perception correlates with future damage[18]. Disease activity can influence survival separately[19,20], and SLICC/ACR damage scores have been correlated with the Health Assessment Questionnaire and the physical function subscale of the Medical Outcomes Survey Short Form 36 (SF-36)[21,22].

Thus damage scored by the SLICC/ACR DI is an important predictor for mortality in SLE and is a practical instrument for clinicians' use.

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