Damage Accrual in Southern Chinese Patients with Systemic Lupus Erythematosus

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ABSTRACT. ***Objective.*** To study the predictive factors of damage accrual in a large cohort of southern Chinese patients with systemic lupus erythematosus (SLE).

Methods. A cohort of consecutive Chinese patients with SLE was recruited in 1998 and prospectively followed for 3 years. Demographic data, disease manifestations and activity, medication use, and damage scores were recorded. Organ damage was assessed using the SLE International Collaborating Clinics Damage Index (SDI), which was scored at study entry and then annually. Disease flares and new damage were recorded during followup visits. Predictive factors of new damage were studied by statistical analysis.

Results. The cohort consisted of 242 consecutive patients with SLE (221 women, 21 men; F:M = 10.5:1). All fulfilled at least 4 American College of Rheumatology criteria for the classification of SLE. At entry, mean age was 35.7 ± 10.7 years and mean disease duration was 75.3 ± 79 months. Ninety (38%) patients had damage. The mean SDI score at year 0 was 0.76 ± 1.3 (range 0–8), and this increased significantly to 1.33 ± 1.7 (range 0–9) at year 3 ($p < 0.001$). The most frequent organ damage at entry was musculoskeletal (26.5%), followed by damage in central nervous system (18.4%), renal (15.1%), and cardiovascular (12.4%) systems. The increase in SDI scores over the 3 year period was primarily caused by the increase in renal, musculoskeletal, and gonadal damage. Twelve patients died. Multiple regression revealed that the number of major disease flares and the use of cyclophosphamide were independent factors predictive of damage accrual. An increase in SDI scores was associated with mortality risk (OR 1.47 per 1 point, 95% CI 1.03–2.11, $p = 0.04$).

Conclusion. The damage scores of our SLE cohort increased significantly over 3 years. Severe disease flares and the use of cyclophosphamide predicted new damage. Increase in damage was associated with mortality risk. Judicious use of immunosuppressive agents to achieve prompt control of disease activity was essential in minimizing damage and improving survival of our patients with SLE. (J Rheumatol 2003;30:1513–9)

Key Indexing Terms:

MORBIDITY	MORTALITY	OUTCOME
RISK FACTORS	CHINESE	ETHNICITY

Systemic lupus erythematosus (SLE) is a multisystemic disease associated with significant mortality and morbidity. With the availability of more potent immunosuppressive agents for disease control, renal replacement therapy for endstage renal disease, and more powerful antibiotics for the control of intercurrent infection, coupled with a more judicious use of medications and meticulous monitoring of complications, the survival of patients with SLE has improved tremendously in the past few decades[1]. The 5 year survival rates of SLE patients in the 1990s have exceeded 90% in recent series[2-4]. Thus, survival rate is no longer a sensitive measure of the outcome of the disease. Objective alternative measures for SLE outcome are necessary. The Systemic Lupus International Collaborating Clinics Damage Index (SDI) was developed by a group of rheumatology experts from around the world to measure cumulative irreversible damage in SLE resulting from both the disease and its treatment[5]. The SDI is a validated tool that has been used in a number of studies of patients with SLE of different ethnicity[6-15].

SDI scores have been shown to increase with time and have been reported to be higher in some non-Caucasian populations[6,10,13,15,16]. Predictors of damage in patients with SLE include older age[7,9,11,15], higher disease activity[7,10,15,17], Hispanic ethnicity[15], greater preexisting damage at enrollment[14], higher dosage of steroid being used[15,18], health perception, and abnormal illness related behavior[8,14,15]. As there has not been any data of damage accrual in southern Chinese patients with SLE, a large cohort of consecutive patients was recruited in 1998 and followed prospectively. Damage accrual was studied and factors predictive of new damage were analyzed by statistical methods.

Patients and methods. Between June and August 1998, a

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cohort consisting of 242 consecutive patients with SLE was enrolled from the rheumatology clinics of Queen Mary and Tuen Mun Hospital for a 3 year prospective study. All patients were ethnic Chinese whose families originated in southern China. All fulfilled at least 4 of the American College of Rheumatology (ACR) criteria for the classification of SLE[19]. Data on demographic characteristics, duration of SLE since diagnosis, clinical manifestations, autoantibodies, and medication use were collected at study entry. Disease activity and flares during followup visits were recorded. Damage was assessed by the SDI[5], scored at study entry (year 0) and then yearly by the same group of investigators throughout.

Assessment of disease activity and flares. Disease activity of SLE was measured using the SELENA-SLEDAI (Safety of Estrogens in Lupus Erythematosus National Assessment – Systemic Lupus Erythematosus Disease Activity Index) instrument, which is a tool to assess lupus activity and flares in the multicenter randomized controlled SELENA trial for the safety of estrogen use in patients with SLE[20]. SLEDAI scores were obtained at entry and during clinic visits by the attending physicians. The SLEDAI scores at disease diagnosis were obtained by chart review in patients whose SLE was diagnosed before recruitment.

Flares of SLE were defined according to the SELENA-SLEDAI instrument. Preliminary evaluation has shown that this instrument is reliable in quantifying disease flare in SLE[21]. Essentially, a severe/major flare was defined as one of the following: (1) increase in SLEDAI score by ≥ 12 points; (2) new/worsening central nervous system (CNS) SLE, vasculitis, nephritis, myositis, thrombocytopenia (platelet count < 50×10^9/l) or hemolytic anemia (hemoglobin < 7 g/dl or drop in hemoglobin by > 3 g/dl) that required a doubling of prednisolone dose or prednisolone > 0.5 mg/kg/day, or hospitalization; (3) any disease manifestations that required augmentation/initiation of prednisolone at a dose > 0.5 mg/kg/day, or the addition of immunosuppressive agents [such as azathioprine (AZA), cyclophosphamide (CYC), methotrexate, and cyclosporin A].

A mild/moderate flare was one that that did not reach the extent of the above but met one of the following criteria: (1) increase in SLEDAI score ≥ 3 points, but < 12; (2) new/worsening skin condition (e.g., cutaneous vasculitis, discoid lesion, photosensitivity, profundus and bullous lesion), mucosal ulceration, serositis, arthritis, or fever; (3) manifestations that required an increase of prednisolone dose to < 0.5 mg/kg/day; or (4) addition of nonsteroidal anti-inflammatory agents or hydroxychloroquine (HCQ).

Measurement of damage. Damage was measured by the SDI[5], a validated instrument consisting of 41 items that measure irreversible organ damage, not related to active inflammation, occurring since the onset of SLE. Each damage item was defined and published in a glossary of terms with the damage index. Manifestations were scored if they had been present for at least 6 months, irrespective of the causes. Repeat events leading to damage in the same organ system were scored up to a maximum of twice provided each event occurred at least 6 months apart. Briefly, damage was defined for 12 organ systems: ocular (range 0–2), neuropsychiatric (0–6), renal (0–3), pulmonary (0–5), cardiovascular (0–6), peripheral vascular (0–5), gastrointestinal (0–6), musculoskeletal (0–7), skin (0–3), and malignancies (0–2). Theoretically, the maximum score that one could accrue was 47 points.

For patients who died during the 3 year observation period, the SDI scores just before death were recorded and used in statistical analyses.

Statistical analyses. Unless otherwise stated, values were expressed as mean ± standard deviation (SD). Comparison of categorical data between 2 groups was by the chi-square test. Comparison of continuous data was by the Student t test for independent samples. When the data did not follow a normal distribution or equal variance could not be assumed, the Mann-Whitney rank sum test was used instead. For comparison of paired data (e.g., the SDI at year 0 and year 3), the Wilcoxon matched pair analysis was used.

The correlation between 2 variables was studied by simple linear regression with the least-squares method and Pearson correlation coefficient (r) was calculated. When the data did not follow a normal distribution, the nonparametric Spearman rank correlation test was used instead.

Multiple regression was used to study the predictive factors for new damage accrual over the 3 year followup period, with various potential covariates being included in the regression equation. The following entry data were considered as predictor variables for new damage in univariate and multivariate analysis: age of disease onset, SLE duration, sex; SLEDAI scores at disease diagnosis, SDI scores at study entry, number of major flares, number of moderate/mild flares, current/past use of prednisone, AZA, CYC and HCQ, autoantibodies (anti-dsDNA, anti-Ro, anti-La, anti-Sm, anti-nRNP, and antiphospholipid antibodies). A stepwise backward elimination procedure was adopted for the multivariate models based on a likelihood ratio test with $p > 0.10$ for removal and $p < 0.05$ for entry of variables. To avoid too many variables entered in the multivariate models given the limited number of observations and events, only the 8 variables with the lowest p values in univariate analysis were included for multivariate analysis.

Statistical significance was defined as a p value < 0.05, 2 tailed. All statistical analyses were performed using the SPSS program, v.8.0 (SPSS, Chicago, IL, USA) for Windows 98.

RESULTS

The cohort consisted of 242 patients with SLE (221 women, 21 men; F:M = 10.5:1). The demographic and clinical characteristics are shown in Table 1. At study entry, the mean age

was 35.7 ± 10.7 years and mean disease duration since diagnosis was 75.3 ± 79 months. Clinical manifestations, in decreasing order of frequency, were musculoskeletal, mucocutaneous, hematological, renal, serosal and neuropsychiatric. Ninety (37.2%) patients had damage at enrollment (year 0) and the mean SDI score was 0.76 ± 1.3 (range 0–8). The distribution of SDI scores was as follows: 40 patients had SDI score of 1; 23 had a score of 2; 16 had 3; 7 had 4; and 4 patients had a score ≥ 5. SDI scores at entry correlated with disease duration (rho = 0.44, $p < 0.001$). At year 3, the number of patients who had damage increased to 133 (55%). The mean SDI scores had increased significantly to 1.33 ± 1.7 (range 0–9) (Wilcoxon matched pair test, $p < 0.001$). The rate of increase of SDI score was 0.19/patient/year.

The mean damage scores in various organ systems of our patients at year 0 (entry) and year 3 (end of followup) are shown in Table 2. At entry, the most frequent organ damage was musculoskeletal (26.5%), followed by CNS damage (18.4%) and the renal (15.1%) and cardiovascular (12.4%) systems. The increase in SDI scores at year 3 was primarily due to the increase in renal, musculoskeletal, and gonadal damage. Within the renal damage domain, a reduction in glomerular filtration rate to < 50% was the most frequent specific item (44%). Osteonecrosis and osteoporotic spinal fractures contributed to 50% and 27%, respectively, of the new musculoskeletal damage. Ovarian failure induced by CYC treatment was the major reason for gonadal damage.

On followup, 173 patients (71%) had disease flares. The mean number of major flares/patient was 0.46 ± 0.74, while that of mild/moderate flares was 0.82 ± 1.01. Twelve patients died during the 3 year period of followup and were regarded as having maximum damage. The causes of death were fulminant infection (6 patients), malignancies (2 patients), severe pulmonary hypertension (one patient), subarachnoid hemorrhage (one patient), cardiac arrhythmia (one patient), and suicide (one patient).

Table 3 shows the demographic and clinical characteristics of patients who did or did not have increase in damage during followup. Variables associated with an increase in damage were higher SDI scores at baseline (study entry), greater number of major flares of SLE and total number of disease flares, as well as current/past use of immunosuppressive agents such as prednisone, AZA, and CYC. Current/past use of HCQ was negatively associated with increase in damage. Patients who had an increase in damage had significantly higher baseline SDI scores, but the increase in SDI scores over the 3 year period was not significantly higher (0.64 ± 0.9 vs 0.54 ± 1.2; $p = 0.47$). On the other hand, a tendency of older age in patients who accrued

Table 1. Demographic and clinical characteristics of our cohort of SLE patients at study entry (n = 242).

Female, n (%)	221 (91.3)
Disease onset, yrs	35.7 ± 10.7
Disease duration since diagnosis, mo	75.3 ± 79
Organ manifestations	
Musculoskeletal, n (%)	209 (86.4)
Mucocutaneous, n (%)	192 (79.3)
Hematological, n (%)	131 (54.1)
Renal, n (%)	111 (45.9)
Serosal, n (%)	44 (18.2)
Neuropsychiatric, n (%)	33 (13.6)
SLEDAI scores at presentation	11.7 ± 5.2
Patients with damage, n (%)	90 (37.2)
SDI scores, n (%)	
0	152 (62.8)
1	40 (16.5)
2	23 (9.5)
3	16 (6.6)
4	7 (2.9)
≥ 5	4 (1.7)

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; SDI: SLICC/ACR Damage Index.

Table 2A. Mean damage scores in our cohort of SLE patients at year 0 and year 3. Figures in brackets represent percentages of damage scores in a certain organ/system with respect to the whole cohort.

SDI Domains	Mean SDI Scores (%)	
	Year 0	Year 3
Ocular	0.07 (8.6)	0.10 (7.7)
Neuropsychiatric	0.14 (18.4)	0.19 (14.2)
Renal*	0.12 (15.1)	0.26 (19.2)
Pulmonary	0.03 (3.8)	0.05 (4.0)
Cardiovascular	0.10 (12.4)	0.14 (10.5)
Peripheral vascular	0.02 (2.2)	0.04 (2.8)
Gastrointestinal	0.01 (1.1)	0.01 (0.6)
Musculoskeletal*	0.20 (26.5)	0.31 (23.2)
Skin	0.02 (2.2)	0.07 (5.0)
Premature gonadal failure*	0.05 (7.0)	0.12 (8.7)
Diabetes	0.02 (2.2)	0.04 (2.8)
Malignancy	0.00 (0)	0.02 (1.2)
Total	0.76 (100)	1.33 (100)

* Statistically significant increase in SDI scores; $p < 0.01$.

Table 2B. Number of patients with damage in various SDI domains at year 0 and year 3.

SDI Domains	Year 0 N (%)	Year 3 N (%)
Ocular	15 (6.2)	21 (8.7)
Neuropsychiatric	29 (12.0)	39 (16.1)
Renal	17 (7.0)	35 (14.5)
Pulmonary	6 (2.5)	11 (4.5)
Cardiovascular	19 (7.9)	26 (10.7)
Peripheral vascular	4 (1.7)	8 (3.3)
Gastrointestinal	2 (0.8)	2 (0.8)
Musculoskeletal	29 (12.0)	49 (20.2)
Skin	4 (1.7)	15 (6.2)
Premature gonadal failure	13 (5.4)	28 (11.6)
Diabetes	5 (2.1)	10 (4.1)
Malignancy	0 (0.0)	5 (2.1)
Any domains	90 (37.2)	133 (55.0)

Table 3. Demographic and clinical characteristics of SLE patients as a function of subsequent damage accrual.

	Further Damage Accrued		
	No, N = 158	Yes, N = 84	p
Female, n (%)	143 (90.5)	78 (92.9)	0.54
Age of SLE onset, yrs	28.2 ± 10.6	31.0 ± 11.5	0.06
Disease duration at entry, mo	71.9 ± 80.2	81.7 ± 75.3	0.36
SLEDAI scores at diagnosis	11.6 ± 5.3	11.9 ± 5.0	0.60
SDI scores at entry (year 0)	0.64 ± 1.23	1.02 ± 1.34	0.03
Patients with damage, n (%)	49 (31)	41 (49)	0.006
No. of major flares/patient	0.27 ± 0.52	0.85 ± 0.94	< 0.01
No. of mild/moderate flares/patient	0.89 ± 1.00	0.69 ± 1.04	0.15
Total no. of flares/patient	1.16 ± 1.07	1.54 ± 1.36	0.02
Past/current use of medications			
Hydroxychloroquine, n (%)	85 (54)	25 (30)	0.01
Azathioprine, n (%)	61 (39)	46 (55)	0.01
Cyclophosphamide, n (%)	35 (22)	43 (51)	< 0.01
Prednisone, n (%)	114 (72)	74 (88)	0.003
Autoantibodies			
dsDNA, n (%)	100 (63)	60 (71)	0.20
Ro, n (%)	93/146 (64)	43/73 (59)	0.49
La, n (%)	15/146 (10)	7/73 (10)	0.86
nRNP, n (%)	36/146 (25)	19/73 (26)	0.85
Sm, n (%)	23/146 (16)	11/73 (15)	0.88
aCLIgG, n (%)	46/131 (35)	16/64 (25)	0.16
aCLIgM, n (%)	14/131 (11)	3/64 (5)	0.18
LAC, n (%)	17/121 (14)	7/55 (13)	0.81

aCL: anticardiolipin, LAC: lupus anticoagulant.

damage on followup was observed. However, when the age of SLE onset was stratified at 50 years, the odds ratio for damage increase for those aged > 50 years compared to those ≤ 50 years was insignificant (OR 2.58, 95% CI 0.56–11.8, p = 0.22). The increase in SDI scores from baseline was also not significantly higher in patients with SLE onset after the age of 50 years than those ≤ 50 years (1.40 ± 1.4 vs 0.56 ± 1.1; p = 0.41).

The univariate and multivariate regression data of the predictive factors for new damage are shown in Table 4. The number of major disease flares and current/past history of CYC treatment were independent predictive risk factors of damage accrual over the 3 year followup period.

For patients who succumbed during the study period, the increase in SDI scores from baseline was significantly higher than for those who survived (1.44 ± 1.1 vs 0.54 ± 1.1; p = 0.04). A separate analysis revealed that the SDI scores at study entry (OR 1.18 per 1 point, 95% CI 0.80–1.74, p = 0.40) did not predict for mortality. The OR for mortality in those patients with damage at study entry (SDI scores ≥ 1) was 2.09 (95% CI 0.62–7.04), which again was not statistically significant (p = 0.24). However, the increase in SDI scores from baseline was found to be a significant predictor of mortality (OR 1.47 per 1 point, 95% CI 1.03–2.11, p = 0.04).

A subanalysis was performed on those patients with disease duration < 12 months at the time of study entry (N =

Table 4. Univariate and multivariate regression data of predictive factors for increase in damage in our cohort of SLE patients. Beta is the regression coefficient.

	Univariate			Multivariate		
Clinical Predictors	Beta	SE	p	Beta	SE	p
No. of major flares, per flare	0.54	0.09	< 0.01	0.49	0.18	< 0.01
Current/past use of CYC	0.66	0.15	< 0.01	0.43	0.17	0.01
Total no. of flares, per flare	0.18	0.06	< 0.01	—	—	—
Current/past use of HCQ	–0.37	0.14	< 0.01	—	—	—
Current/past use of Pred	0.45	0.17	< 0.01	—	—	—
Current/past use of AZA	0.28	0.14	0.05	—	—	—
Positive aCL-IgG	–0.29	0.18	0.10	—	—	—
Positive anti-nRNP	0.27	0.17	0.12	—	—	—

SE: standard error, CYC: cyclophosphamide, HCQ: hydroxychloroquine, Pred: prednisone, AZA: azathioprine, aCL: anticardiolipin.

59). There were 54 women (91.5%). The mean age of SLE onset was 31.5 ± 10.3 years. Seven (12%) patients had damage at enrollment and the mean SDI score was 0.15 ± 0.45. At the end of 3 years, 19 (32.2%) patients had SDI scores ≥ 1 and the mean SDI scores increased significantly to 0.55 ± 1.0 (Wilcoxon matched pair test, $p < 0.001$). Fifteen patients had increase in SDI scores compared with baseline and there were 3 deaths in this subcohort. Due to the small sample size and the limited number of events, no predictive factors of damage accrual or mortality could be identified. However, major flares occurred more frequently in patients who had increase in damage scores during the study period compared to those who did not (mean number of major flares 0.73 ± 0.88 vs 0.28 ± 0.45; $p = 0.07$). Those patients who succumbed during the study period tended to accrue more damage before death compared to those who survived (increase in SDI scores 1.50 ± 0.71 vs 0.39 ± 0.95; $p = 0.25$).

DISCUSSION

This is a longitudinal observational study on damage accrual of a large cohort of southern Chinese patients with SLE. Our results confirmed the observation that damage in SLE accumulates with time, correlates with disease duration, and contributes significantly to disease morbidity and mortality. Serious manifestations at baseline, increasing number of major disease flares, and the use of CYC were associated with new damage accrual in our patients.

It has been well recognized that the prognosis of SLE is worse in certain ethnic groups. Lupus nephritis runs a more aggressive course in American Blacks and the rate of endstage renal failure is significantly higher than in Caucasians[22]. The overall survival of SLE is poor in the African Caribbeans, and Hispanics, Africans, and Indians residing in America[3,23-25]. Low socioeconomic status (poverty) and abnormal illness behavior may contribute to the poor outcome of SLE in these ethnic groups[15,26]. Asian SLE patients residing in the United States and the United Kingdom have also been reported to have more serious organ system manifestations and higher mortality rates[27,28]. However, a recent study reported a similar 5 year survival rate in Southern Chinese SLE patients and in Caucasians[4]. This may indicate that the prognosis of SLE in Chinese may not be significantly worse than that of Caucasians.

Damage accrual in SLE may also show interethnic differences. A recent study described that Hispanic SLE patients residing in the US accrued more damage than the Caucasians[15]. There have not been any publications examining damage accrual in Chinese SLE patients. In our study, the mean SDI score in our cohort was 1.33 at the end of followup and the increment over 3 years was 0.56 per patient. This figure is not impressively different from those observed in Caucasians[7,8,14,15], although direct comparison is not feasible because of the differences in study design and patient selection at entry. Nevertheless, it appears that the course and outcome of SLE is not particularly bad in Southern Chinese in terms of damage accrual and mortality.

In addition to an increase in the number of patients who developed renal insufficiency, the main contributors to damage increase in our cohort were osteonecrosis and gonadal failure. While more aggressive therapeutic regimens are needed to preserve renal function in patients with severe nephritis, the use of corticosteroids and cytotoxic drugs may lead to more damage.

Disease activity has been described as the most important factor for damage in SLE[7,10,15,17]. This is expected because damage in SLE is defined as that caused by either the disease itself or its treatment. However, as disease activity in SLE tends to fluctuate with time and some patients may have a chronic active disease pattern[29], the disease activity score at a single time point is not a good indication of the overall activity. This is illustrated by our observations that the SLEDAI scores at disease diagnosis did not predict damage. Measurement of the cumulative disease activity by calculating the area under the curve (AUC) of the serial SLEDAI scores over time is more accurate for assessing the overall activity in individual patients. A recent study showed that cumulative disease activity over time was the single best predictor of damage in a cohort of patients with childhood SLE[17]. Although data on AUC were not available in our study, the number of major disease flares is a reasonable estimate of disease activity and severity in our patients. The observation of the number of severe disease flares as the most significant independent predictor of damage accrual in our patients indicates that disease activity is an important determinant for morbidity in patients with SLE.

Age has been shown to influence disease activity and damage in SLE. Childhood onset SLE tends to run a more aggressive disease course, with more frequent and serious nephritis[30-32], and has more damage accrual[17]. Conversely, late onset SLE, defined as first onset of disease after age 50 years, has been reported to have a more insidious course, less major organ involvement, particularly nephritis, less hypocomplementemia, less disease activity, and fewer relapses on followup[33-36]. However, a very recent study described that patients with late onset SLE (≥ 54 years) had higher damage scores and a different pattern of damage compared to younger onset controls (< 40 years) matched for sex and ethnic origin[37]. Whether the difference in damage accrual and pattern between the late and younger onset patients reflected the effect of age *per se* remains to be confirmed. Indeed, increasing age has been shown in other studies to be a risk factor for damage in SLE[7,9,11,15]. However, we could not confirm older age as an unfavorable factor for damage accrual. The insignificant result could be accounted for by the small number of patients with late onset SLE in our cohort (N = 12).

The observation of current/past use of CYC as a risk

factor for damage accrual in our study is of interest. This may reflect that SLE patients with more serious disease manifestations that warrant more aggressive treatment are more prone to new damage. Indeed, the use of CYC *per se* is associated with gonadal toxicities and contributed significantly to new damage scores in our cohort.

Preexisting damage has been shown to predict for future damage in SLE[14]. Again, this may merely reflect that patients with more serious disease manifestations and hence more baseline damage are more prone to further disease and treatment related complications. In our study, although patients who had damage accrual had significantly higher baseline SDI scores, the increment in damage scores was not significantly different between those with and those without damage at entry. Regression analysis also failed to show any correlation between the baseline SDI scores and new damage accrual during the 3 year study period. Table 5 summarizes the main findings of previous studies on damage in SLE.

Finally, damage has been shown to predict for SLE mortality in some studies[6,12,13,25,38]. Although the SDI scores at entry were not found to predict death in our cohort, the increase in SDI score from baseline was significantly higher in those patients who died during the study period. A recent study showed that early damage within the first year of diagnosis of SLE was a significant predictor of mortality at 10 years[38]. Due to the small proportion of patients with early damage in our cohort and the limited number of deaths, early damage could not be shown to predict mortality in this subset of patients. Expansion of the sample size and a longer period of observation are needed to address this issue. Nevertheless, minimizing damage is mandatory to improve the overall survival of patients with SLE.

The damage scores of our cohort of southern Chinese patients with SLE increased significantly over a 3 year period of followup. Most new damage was attributed to renal disease, musculoskeletal complications, and gonadal failure. Damage accumulated with time and correlated with disease duration. Major disease flares and the use of cyclophosphamide predicted new damage. Increase in damage was associated with mortality risk. Judicious use of immunosuppressive agents to achieve prompt control of

Table 5. Main findings of studies on damage in SLE patients.

Author	Study Design	No. of Patients	Ethnicity	Main Findings
Stoll 1996[6]	R	80	Caucasians, Afro-Caribbeans, Asians	Non-Caucasians accrued more damage than Caucasians, renal SDI scores at first year predicted renal failure at 10 years, pulmonary scores at first year predicted mortality at 10 years
Hanly 1997[8]	R	96	Caucasians	No association between SDI scores and SLEDAI scores or SF-20 subscales except for healthy perception
Karlson 1997[9]	R, M	200	Caucasians and Blacks	Longer disease duration, older age, poor nutrition, and higher disease activity at diagnosis associated with damage
Stoll 1997[7]	R	141	Caucasians, Afro-Caribbeans, Asians	SDI subscores correlated with disease activity in the corresponding organs, damage associated with increasing age, weak association between health perception and damage in individual organs
Nossent 1998[10]	R	90	Caucasians	SDI scores correlated with number of flares and overall disease activity (SLEDAI score >10), but did not predict mortality
Voss 1998[12]	R, M	NS	Caucasians (Danish)	Patients who died accrued more damage before death
Zonana-Nacach 1998 [11]	R	210	Mexicans	Damage increased over time, associated with older age, longer disease duration, and increasing number of ACR criteria for SLE
Gladman 2000[13]	R, M	1297	Caucasians, Blacks	SDI scores increased with time and disease duration, higher SDI scores in patients who went on to die
Stoll 2000[14]	P	141	Caucasians, Afro-Caribbeans, Asians	Total SDI scores, SF-20, health perception predicted further damage after 3 years
Zonana-Nacach 2000[18]	P	539	African Americans, Caucasians	Cumulative steroid dose associated with osteoporotic fractures, symptomatic coronary heart disease, and cataracts, exposure to high dose steroid associated with increase risk of osteonecrosis and strokes
Alarcon 2001[15]	P	258	Hispanics, African Americans, Caucasians	Hispanics accrued damage more rapidly. Steroid use, no. of ACR criteria, disease activity, age, and abnormal illness behaviors contributed to damage
Rahman 2001[38]	P	263	Mostly Caucasians	Early damage at initial assessment predicted mortality at 10 years
Brunner 2002[17]	R	66	Caucasians, Blacks Asians	Ongoing disease activity leads to disease damage. High-dose steroids, presence of aPLantibodies, and acute thrombocytopenia predicted increase in damage
Present study	P	242	Southern Chinese	Damage accumulated over time. Major disease flares and use of CYC predicted further damage. Increase in damage scores was associated with mortality

R: retrospective, M: multicenter, P: prospective, NS: not stated, aPL: antiphospholipid, SF-20: Medical Outcomes Study Short-form 20 index.

disease activity was essential in minimizing damage and improving survival of patients with SLE.

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